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Original Communications

STUDIES IN OLEOTHORAX

I. THE BACTERIOSTATIC ACTION OF OILS ON THE TUBERCLE BACILLUS

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SEVERAL of the unsaturated fatty acids have been reported to be bactericidal for the tubercle bacillus. Négre[1] reported that the bactericidal action of the unsaturated fatty acids of the lower homologue series depends upon the number of double bonds, their solubility in water, and their adsorption to the bacterial cells. Although oleic, linoleic, and linolenic acid were bactericidal, their soaps were not. However, these fatty acids did not retard the development of tuberculosis in guinea pigs when injected with the infecting dose. Similar findings had been previously reported by Boissevain.[2] Clerc[3] reported that the vapors of gomenol inhibited the growth of *Mycobacterium tuberculosis* on solid media. Tuberculous tissue emulsified with gomenol and injected into guinea pigs produced a low-grade disease. Platonov[4] found that cod-liver oil had a marked lytic action on the human tubercle bacillus, retarded its growth, and lowered its virulence. When virulent human tubercle bacilli were incubated with cod-liver oil for forty days and then injected into guinea pigs, a low-grade fibrous type of disease was produced. Leusden and Derlich[5] determined the bactericidal and bacteriostatic action of cod-liver oil and vitamin A enriched cod-liver oil for various organisms. They concluded that the active principle in the oils is a water-soluble compound, active only when the bacteria are in contact with the oil in an environment free from water. They also suggested that the unsaturated fatty acids may not be wholly responsible for the inhibitory action, but that vitamin A may also play a role in bacteriostasis.

Solomides[6] found that when peanut oil was added to well-developed colonies of *Myco. tuberculosis* grown on glycerinated potato medium, a change in staining character and in morphology, ending in complete lysis, occurred. When peanut oil was incorporated in the medium, growth of the bacilli was markedly delayed. A similar change in morphology and staining characteristic was noted by Laporte and Bretey[7] when dried tubercle bacilli were suspended in mineral oil.

From the Boehne Hospital.
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METHODS

The media used in this experiment were Long's synthetic medium, Corper's egg medium, and glycerol-peptone agar. Peanut oil and cod-liver oil were added to these media, which were emulsified. A homogeneous emulsion was not obtained, since some of the oil collected on the surface after a few days. The pH of the medium was adjusted to pH 7.0, and inoculated with a loopful of a ten-day old culture of the respective organisms grown on Long's synthetic medium.

EXPERIMENTAL

Effect of Oil on Growth.—Tables I and II show the growth of the H_{37}, bovine, and avian types of *Myco. tuberculosis,* when peanut oil and cod-liver oil were added to the media in increasing concentrations. Growth was delayed in the first week, as compared with the control cultures, although after two weeks the amount of growth was almost equal to that in the control cultures. No further growth occurred after two weeks. In the media containing peanut oil there was considerable growth at the bottom of the flasks, while with cod-liver oil there was none. There was a striking difference in the appearance of the growth in the media with peanut oil and cod-liver oil. The pellicle in the flasks with peanut oil grew between the oil droplets and was slightly yellowish, while the growth in the flasks with cod-liver oil occurred in greater clumps. It was impossible to separate the oil from the bacterial cells by centrifugation. Some of the oil adherred to the bacteria even after being washed with acetone and ether. In the cultures with cod-liver oil, the oil and the mass of cells turned brown at the end of two weeks. The color deepened with the age of the culture, although no additional growth occurred. The cultures with cod-liver oil also became more acid than those with peanut oil, although growth was less with cod-liver oil than with peanut oil. This increase in acidity is probably due to autolysis of the cells and breakdown of the cod-liver oil.

After growth for four weeks on Long's medium with various concentrations of cod-liver oil and peanut oil, transfers were made to Corper's egg medium and to glycerol-peptone agar. The results in case of the media with peanut oil appear in Table III. It will be noted that subcultures of the human and avian strain from concentrations of peanut oil up to 10 per cent grew on Corper's medium, but that subcultures from the bovine strain did not grow when the concentration of oil exceeded 2 per cent. Subcultures of all the strains from Long's medium with cod-liver oil failed to grow on either Corper's egg medium or glycerol-peptone agar.

In further experiments, the oils were incorporated in Corper's egg medium. Cod-liver oil, peanut oil, and gomenol were homogenized with the egg yolks in such proportions that after the addition of 25 per cent water and 5 per cent glycerol, the final concentrations of the oils were 1, 2, 5, and 10 per cent. The medium was inspissated on three successive days. The slants were inoculated with two-week old cultures of the H_{37}, bovine, and avian strains of *Myco. tuberculosis,* and incubated at 37.5° C. It will be noted (Table IV) that the bovine type was the most sensitive and the avian type was the least sensitive, with the H_{37} strain in an intermediate position. Even in 1 per cent concentration, cod-liver oil completely inhibited the growth of all three types of *Myco. tuberculosis.* Two per cent peanut oil required to inhibit the avian type was not determined, but was is excess of 10 per cent. The bovine type, however, would not grow when the concentration of peanut oil exceeded 1 per cent. Both

TABLE I. GROWTH IN LONG'S MEDIUM WITH

TABLE I. GROWTH IN LONG'S MEDIUM WITH 1, 2, 5, AND 10 PER CENT COD-LIVER OIL ADDED

WEEKS	1 PER CENT			pH			2 PER CENT			pH			5 PER CENT			pH			10 PER CENT			pH			CONTROL			pH		
	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A
1	–	–	–	7.2	7.2	7.2	–	–	–	7.2	7.2	7.2	–	–	–	7.2	7.2	7.2	–	–	–	7.2	7.2	7.2	+	–	+	7.0	7.2	7.0
2	+	+	+	6.6	7.2	6.4	Sl.	–	–	6.4	7.2	6.6	+	+	+	5.6	7.2	4.9	+	+	+	5.0	7.2	4.9	+++	++	+++	6.9	7.3	6.8
3	No further growth																								Continued growth					

TABLE II. GROWTH IN LONG'S MEDIUM WITH 1, 2, 5, AND 10 PER CENT PEANUT OIL ADDED

WEEKS	1 PER CENT			pH			2 PER CENT			pH			5 PER CENT			pH			10 PER CENT			pH			CONTROL			pH		
	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A	H_{37}	B	A
1	–	–	–	7.2	7.2	7.2	–	–	–	7.2	7.2	7.2	–	–	–	7.2	7.2	7.2	–	–	–	7.2	7.2	7.2	+	–	+	7.0	7.2	7.0
2	++	++	++	6.8	7.0	6.9	+	++	++	6.9	7.0	7.0	+	–	++	7.0	7.0	7.0	–	–	+	7.2	7.2	7.2	+++	++	+++	6.9	7.3	6.8
3	No further growth																								Continued growth					
4																														

TABLE III. GROWTH OF SUBCULTURES FROM MEDIA WITH ADDED PEANUT OIL ON AGAR AND ON CORPER'S MEDIUM

H_{37}								BOVINE								AVIAN							
1 PER CENT		2 PER CENT		5 PER CENT		10 PER CENT		1 PER CENT		2 PER CENT		5 PER CENT		10 PER CENT		1 PER CENT		2 PER CENT		5 PER CENT		10 PER CENT	
A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C	A	C
+	+	–	+	–	+	–	+	–	+	–	+	–	–	–	–	+	+	+	+	–	+	–	+

A, Agar.
C, Corper's medium.

TABLE IV. GROWTH OF H_{37}, BOVINE AND AVIAN TYPES ON CORPER'S MEDIUM, WITH PEANUT OIL, COD-LIVER OIL, AND GOMENOL ADDED; APPEARANCE OF GROWTH IN DAYS

PEANUT OIL				COD-LIVER OIL			GOMENOL			APPEARANCE OF GROWTH IN DAYS WITH PEANUT OIL AND GOMENOL				
PER CENT	H_{37}	BOVINE	AVIAN	H_{37}	BOVINE	AVIAN	H_{37}	BOVINE	AVIAN	H_{37} (DAYS)	BOVINE (DAYS)	AVIAN (DAYS)	CONTROL (DAYS)	
1	+	+	++	–	–	–	–	–	–	7	21	7		
2	+	–	–	–	–	–	–	–	–	21	0	10	H_{37}	7
5	–	–	–	–	–	–	–	–	–	0	0	14	Bovine	10
10	–	–	–	–	–	–	–	–	–	0	0	28	Avian	6

peanut oil and gomenol in the concentrations that allowed growth caused a delay in its appearance.

It was noted that subcultures from Long's medium with cod-liver oil failed to grow on Corper's medium, although a large inoculum was used. At the end of six weeks the inoculum was still present on the slants. The virulence of this material was tested by injecting 0.01 mg. of the organisms subcutaneously into the groin of two guinea pigs. The same dose of strain H_{37} not exposed to cod-liver oil was injected into the groin of two control animals. All of the animals were killed in six weeks. At autopsy there was no difference in the type or extent of the disease in the animals. This demonstrates that the H_{37} strain did not lose its viability or virulence during the prolonged contact with cod-liver oil. Most probably the oil adsorbed by the bacteria interferes with the respiratory enzymes and inhibits growth on the culture media, while after injection into the animal body the oil is removed by the body fluids and the organisms are free to develop.

Experiments were also conducted to observe the effects of cod-liver oil, peanut oil, and gomenol on the colony morphology and staining properties of the H_{37} strain and the bovine type of tubercle bacillus. Six-week old cultures of these types with well-developed colonies were flooded with cod-liver oil, peanut oil, and gomenol. The tubes were left in a slanting position to cover the colonies with oil for twenty-four hours at 37.5° C., after which the oil was shaken down to the bottom of the tubes, and they were incubated one week. After contact with the oils for twenty-four hours, the colonies had a moist, glistening appearance with a pasty consistency. They were readily emulsified. Prolonged incubation did not result in the lysis described by the workers in similar experiments with gomenol and peanut oil. The bacteria did not lose their acid-fastness, nor was there a marked increase of the acid-fast granules. The majority of the organisms appeared as short, acid-fast coccobacilli with occasional branching and beaded forms with deeply staining granules and colorless vacuoles. A few nonacid-fast rods were found in the gomenol flooded cultures. After the one-week incubation period, there was partial lysis of the colonies, their edges becoming indistinct. Subcultures from the edges of the colonies of the H_{37} strain on Corper's egg medium failed to grow in six weeks, but when the inoculum was taken from the center of the colonies, growth was obtained. This suggests that growth was inhibited by the oil adherent to the cells.

Effect of Oil on Virulency: A human strain of *Myco. tuberculosis* isolated from sputum in this laboratory, of which 0.01 mg. kills guinea pigs in six to seven weeks when injected into the groin subcutaneously, was treated in the same way with cod-liver oil, gomenol, and peanut oil. It was impossible to demonstrate a loss of virulences of this strain of the human tubercle bacillus by the action of these oils. Highly positive sputum with approximately 100 tubercle bacilli per oil immersion field was incubated with equal parts of cod-liver oil, peanut oil, and gomenol at 37.5° C. for six weeks. Since, after this incubation, the sputum still contained other viable organisms besides the tubercle bacillus, it was digested by Hank's method and planted on Corper's medium. Growth was noted in three weeks and guinea pigs injected with 0.01 mg. of the organisms died within six weeks.

Aspirated purulent pleural exudate, to which 0.01 mg. of the isolated virulent human strain per cubic centimeter of fluid was added, was similarly incubated with these oils. Cultures on Corper's medium were all positive in three weeks, and the organisms retained their usual virulence when injected

into guinea pigs. There was no loss in acid fastness. The morphology of the organisms was altered, however, there being numerous branching and very granular and beaded forms. Nonacid-fast granules were not found.

Purulent exudates aspirated from patients with tuberculous empyema in whom oleothorax with cod-liver oil or peanut oil had been established were repeatedly tested for the viability and the virulence of the tubercle bacilli in them. In every case, regardless of the length of time the oil had been in the chest, the organisms recovered were virulent. It is evident that the observations do not confirm those reported by Boissevain,[2] Platonov,[4] and Solomides.[6] To test this further, Leusden and Derlich's[5] experiment on the effect of cod-liver oil on *Escherichia coli* was repeated. These workers gave four to eight hours as the lethal time when *Esch. coli* was exposed to cod-liver oil. We used an atypical acid- and gas-producing strain isolated from feces in this laboratory. A loopful from a twenty-four-hour old culture was well mixed with 10 c.c. of cod-liver oil. The first count after three hours was 1,000,000 colonies per cubic centimeter when grown on heart infusion agar. No decrease in the count was observed at the end of eight hours, and in twenty-four hours the count was 153,000 per cubic centimeter, at which time incubation was discontinued.

COMMENT

Cod-liver oil and peanut oil have no effect on the virulency of the tubercle bacillus. This difference in results with other investigators can be due to a marked difference in the resistance of the bacterial strains to cod-liver oil used by the other workers and ourselves, or by a difference in the oils employed. It is more probable that the oils available today are more highly purified than those of a decade ago, and have been freed from the substances responsible for the bacteriolytic action. Gomenol was included in this study because it has been extensively used in "disinfection" oleothorax. Cod-liver oil and peanut oil were studied, because of the reports of their inhibitory effect on the tubercle bacillus. We concur that these oils have an inhibitory action on the growth of the tubercle bacillus. However, the subsequent growth of the organisms on a rich medium and their normal virulence when injected into guinea pigs indicates that the oils adherent to the tubercle bacilli inhibit their growth by a physical rather than by a chemical action.

SUMMARY

1. The bacteriostatic action of peanut oil, cod-liver oil, and gomenol for the H_{37} strain, and the bovine and avian types of *Myco. tuberculosis,* was determined.

(a) Peanut oil is inhibitory for H_{37} and other virulent human strains in a concentration of 5 per cent; for the bovine type in a concentration of 2 per cent; for the avian type the limit of tolerance was not determined, but it is greater than a concentration of 10 per cent.

(b) Cod-liver oil is bacteriostatic for the human, bovine, and avian types of *Myco. tuberculosis* in 1 per cent concentration.

(c) Gomenol is bacteriostatic for both human and avian types of *Myco. tuberculosis* in 5 per cent concentrations. Complete inhibition of the bovine type occurred in 1 per cent concentration.

2. Prolonged incubation of the H_{37} strain and a virulent human strain isolated in this laboratory with peanut oil, cod-liver oil, and gomenol does not alter the virulence or the acid-fastness of the organisms, although the colony morphology is altered.

3. The complete lysis of colonies by the oil studied was not observed.

4. After exposure of the human and bovine strains to the inhibiting effect of oils, a rich medium is required for growth.

5. It is suggested that the oils adherent to the tubercle bacilli inhibit the growth of this bacillus by a physical rather than a chemical action.

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STUDIES IN OLEOTHORAX

II. The Use of Oils in Disinfectant Oleothorax and in the Re-expansion of the Lung in Tuberculous Empyema (Preliminary Report)

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THE development of effusions and empyemas is an inevitable complication in any series of patients with pulmonary tuberculosis, who are treated with or without pneumothorax. Few patients escape at least a small effusion during pneumothorax treatment. Opinions vary as to when an effusion becomes an empyema. Simple effusions harboring tubercle bacilli frequently disappear, while secondarily infected empyemas present difficult surgical problems.

Simple effusions, without the presence of tubercle bacilli, are satisfactorily treated with frequent aspirations and the maintenance of negative intrathoracic pressures. If tubercle bacilli persist, with or without varying degrees of purulency, approximation of the pleural surfaces is ultimately demanded. We consider the empyema cavity of more immediate importance than the pathology in the underlying lung, not only because of the toxicity of the patient with an early empyema, but also because the extent of the surgery necessary for the lung pathology is generally less formidable than that required for the empyema.

Tuberculous empyemas have been treated with saline, merthiolate, azochloramid, neoprontosil, formalin in glycerin, ethyl morrhuate, Lugol's solution, Dakin's solution, gomenol, various aniline dyes, and bland oils. In 1922, Bernou[1] introduced oleothorax in the treatment of pulmonary tuberculosis.

From the Boehne Hospital.
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Matson[2] was the first American investigator to report a large series of patients treated with oleothorax. In fifty cases of tuberculous empyema treated with gomenolized oil, satisfactory results were obtained in 60 per cent. The empyema cleared and the collapse was maintained by either air insufflations or oil blockade. He advised (1) complete evacuation of pus, (2) thorough cleansing of the pleural cavity, and (3) disinfection oil bath of the entire serosa. An exhaustive discussion on the subject of oleothorax was contributed by Joannides,[3] although no clinical results were presented. Browning, Dundon, and Ray[4] advised using 4 per cent cottonseed oil, with which they treated forty-eight patients with tuberculous empyema. The pus disappeared in 68 per cent of the cases under treatment, but the end results were not published at that time. In the discussion of the mechanism by which oleothorax stops fluid formation, these workers came to no definite conclusion.

Etiology.—The etiology of tuberculous empyema has been the subject of much discussion. The most commonly accepted view is that the pleural space becomes infected from ulceration of a subpleural focus. The frequency with which such subpleural lesions are seen at post-mortem supports this view. Coryllos[5] presented impressive evidence that all cases of tuberculous empyema, whether they develop as primary purulent effusions, or from previously clear effusions, are caused by pleuropulmonary communications, due to caseation and ulceration of subpleural tuberculous foci. The essential factor, whether such transient communications exist or not, is the ulceration of a caseous subpleural focus. The greater incidence of both serous effusions and empyemas, in mechanically unsatisfactory pneumothoraces, is explained by the fact that the adhesions which prevent collapse and the effusion or empyema are caused by subpleural tuberculous foci.

Irritant Oils.—Our interest in the use of oleothorax, in the treatment of tuberculous empyema and in effecting the re-expansion of the lung, was stimulated by the successful resolution of a tuberculous pyopneumothorax with subsequent re-expansion of the lung by oleothorax with cod-liver oil, rather than by the use of a bland oil. Since then, we have used both cod-liver oil and peanut oil, in a similar manner, with successful end results. When Matson[2] reported his series of oleothorax cases, he stated specifically that mineral oil and cotton-seed oil were employed because of their slight irritant action on the pleura. These oils, with olive oil, have been employed by almost all subsequent workers. Both cod-liver oil and peanut oil are rather markedly irritating to the pleura, and have not been employed previously for routine oleothorax therapy. We employed these oils in a routine manner only after extended study of their effects in guinea pigs and in a few patients.

An appreciation of the causative role of subpleural caseous foci is vital in the treatment of tuberculous empyema. The infection of the pleura is secondary to the parenchymal pulmonary infection. This infection, caused by the tubercle bacillus, cannot be disinfected by a strong enough concentration of any chemical without irreparable injury to the pleurae. Thus, to speak of "disinfection" of the pleurae by irrigation or instillation of some chemical, in a manner analogous to the cleansing of a skin surface, is wholly erroneous. The pleurae are, therefore, subject to constant reinfection until the subpleural foci heal, unless they are separated from the subfocal infection by an effective barrier, such as oil. The entire pleural surface must be covered with oil to prevent spread of the infection, until sufficient inflammatory reaction walls off the foci and approximates the surfaces of the two pleurae.

Histologic Changes in the Pleura.—In guinea pigs killed twenty-four hours after intrapleural instillation of peanut oil, there is found a creamy exudate containing flakes of fibrin. The cells in the exudate are practically all polymorphonuclear leucocytes. Examination of prepared sections of the parietal pleura shows a layer of polymorphonuclear leucocytes enmeshed in strands of fibrin on the surface, marked engorgement of the blood vessels of the pleura, with diapedesis of leucocytes and perivascular cellular infiltration. Examination of the lung and visceral pleura shows a similar change in the pleura, with marked engorgement of the capillaries of the subjacent alveoli, and collection of fluid, leucocytes, and a few red blood cells within them.

In a moribund patient with extensive retroperitoneal lymphosarcoma, 100 c.c. of peanut oil were introduced into the pleural space after preliminary pneumothorax. At autopsy twenty-four hours later, the pleural space contained 300 c.c. of opaque yellowish fluid with fibrin clots, and both the parietal and visceral pleura were covered with a thick, shaggy, yellowish exudate which was difficult to rub off. The exudate contained largely neutrophiles, most of which were broken down, and a few macrophage cells and lymphocytes. The pleurae were covered with a thick layer of fibrin and polymorphonuclear leucocytes. Histologically, the capillaries of the underlying lung were engorged with blood, and the alveoli were filled with edematous fluid.

A similar experiment, in a patient with metastatic carcinoma of the liver, decompensated heart disease, and tuberculous pleural effusion, was done with cod-liver oil. At autopsy three days later, a similar, more organized exudate was seen, with many fibrinous adhesions. The histologic changes in the pleurae were similar to those obtained with peanut oil. The changes in the pleura, produced by oil over a prolonged time, also were observed at autopsy.

A patient, in whom oleothorax with cod-liver oil was produced to control a seropurulent tuberculous effusion died twenty-three months later with tuberculous peritonitis and enterocolitis. The pleural space, at autopsy, contained oil which was almost as clear as when it was introduced. There was no fluid. Beneath the oil, there were large, cheesy flakes of debris, some of which were loosely adherent to the pleural surface. No recognizable cells were found in these clumps. The parietal pleura averaged 2 mm. and the visceral pleura 1½ mm. in thickness. Although the underlying lung was riddled with caseous and caseoulcerative nodules, these were walled off from the pleural space by the thickened pleura. With the exception of the loosely adherent clumps of debris, the pleural surfaces were clear.

Cellular Reaction to Oil.—Before the introduction of peanut and cod-liver oil, the type and number of cells in the fluid or exudate were determined. The irritant oil was then introduced and the cellular reaction at intervals from twenty-four hours to several weeks was observed. In general, the most marked reaction is obtained in those patients with a serofibrinous, or mildly seropurulent fluid. In these cases, on aspiration twenty-four hours after instillation of oil, an opaque, milky to creamy fluid is obtained, which on centrifugation separates into a lower layer composed of cells and cellular debris, an intermediate layer of fluid, and an upper layer of emulsified fluid and oil. The cells are mostly polymorphonuclear leucocytes (65 to 85 per cent in different specimens), the remaining cells being small lymphocytes with occasional monocytes and eosinophilic polymorphonuclears. After forty-eight hours many of the cells show degenerative changes. There are a few more small lymphocytes and monocytes, and a few less polymorphonuclear leucocytes.

One week after the instillation of oil there is much cellular debris and many degenerated polymorphonuclear leucocytes. Of the intact cells, about 50 per cent are polymorphonuclear leucocytes and 40 per cent are small lymphocytes, with a few monocytes, large lymphocytes and eosinophiles.

Two weeks after oil instillation, the fluid is much less turbid and thereafter gradually becomes clear, especially when the tubercle bacilli disappear. Almost all of the cells are small lymphocytes, with a few polymorphonuclear leucocytes and monocytes.

The reaction to peanut oil in cases of empyema with markedly purulent fluid is much less pronounced, probably because the pleural reaction is already maximal. Periodic examination after oil instillation in these patients shows a progressive decrease in the polymorphonuclear leucocytes and an increase in the number of small lymphocytes. The fluid one week after oil instillation is much thinner, and contains fewer intact cells. After about two months the fluid may contain ropy, tenacious mucous shreds, but almost no cells.

A qualitatively similar, but quantitatively more severe cellular reaction, was observed following the instillation of cod-liver oil. Similar but less striking responses are observed after intrapleural instillation of mineral oil, olive oil, and cottonseed oil. The quantitative variations in the pleural response are determined by the degree of the irritant action and the extent of the inflammatory reaction of the pleurae at the time the oil is instilled. This inflammatory reaction stimulates the production of a pleuritis which gradually approximates the two pleural surfaces.

Clinical Reactions.—The immediate symptomatic reaction to oleothorax is usually most marked in those patients with serofibrinous or mildly seropurulent effusions, and least marked in those with a very purulent empyema. Early symptoms occur within four to eight hours after oil is introduced, when most patients complain of a pain in the chest. This is variously described as a dull aching pain, a burning sensation, or occasionally as an acute pain. It rarely persists more than forty-eight hours and seldom requires analgesics for relief. It is much less marked or absent with subject instillations of oil. Accompanying this pain there is usually a feeling of malaise and a rise in temperature, usually not exceeding 1°.

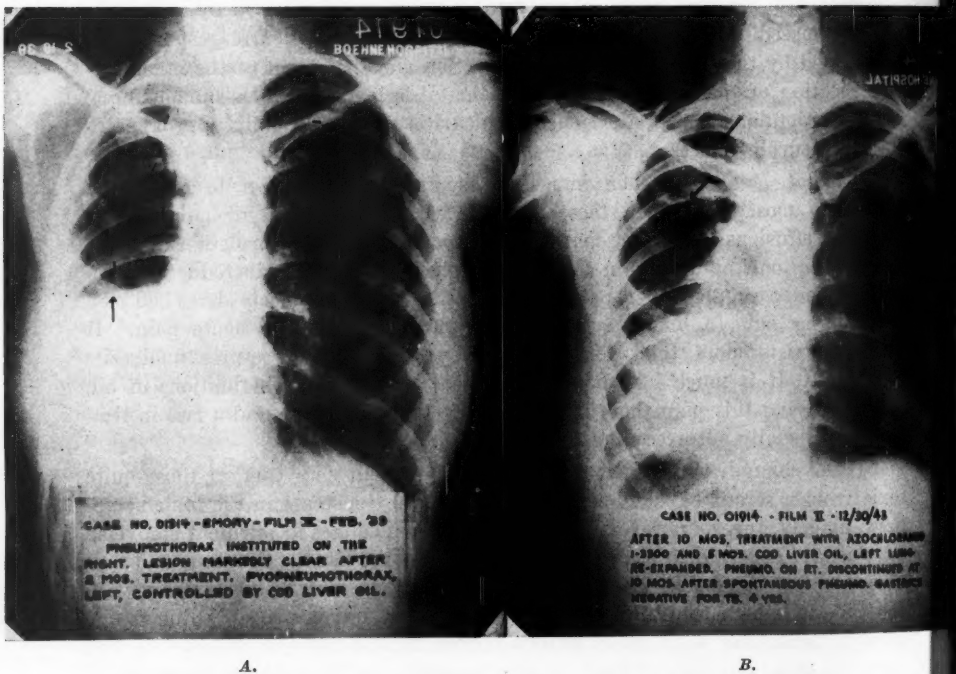
Later changes observed in patients with purulent empyema, or those quite toxic from a serous effusion, consist of a significant decrease in the toxic symptoms, namely, fever, anorexia and malaise. These changes in purulent empyema have always occurred in our series of cases. They are usually dramatic and take place within four weeks after the oil is injected. It corresponds roughly with the time at which the fluid ceases to be purulent and is probably due to the pleural thickening with inflammatory obliteration of the lymphatics. In two cases the small quantity of fluid remains purulent, but the patients are symptom free. With the improvement in this toxic state, there is usually a marked increase in general well-being and an improvement in appetite, accompanied by a gain in weight. The patient becomes a much better surgical risk, should surgery become necessary.

REPORT OF CASES

The following cases are typical of those treated with an irritant oil. Cases 1 and 2 represent obstinate cases of tuberculous empyema, which ordinarily demand extensive thoracoplasty. Case 3 represents a secondarily infected tuberculous empyema, which has a minimal amount of underlying lung pathology.

Case 4 is a report of a patient who had a fairly clear effusion, with tubercle bacilli present. At the present time tubercle bacilli are absent and the oil is being withdrawn gradually to allow the lung to re-expand. Case 5 demonstrates a problem similar to Case 4, except that the underlying lung requires a longer period of collapse and the continuation of a therapeutic oleothorax. Tubercle bacilli are absent, which indicates the subpleural focus is healed.

Case 1.—In December, 1937, this patient had infiltration with cavitation in the left upper lobe, and in second and third interspaces in the right upper lobe. The sputum was positive for tubercle bacilli, and pneumothorax was instituted on the left. An intrapleural pneumolysis was performed in January, 1938, on this side. Fig. 1*A* (taken Feb. 19, 1939) shows a tuberculous empyema of ten months' duration. Azochloramid 1:3300 was used for ten months for irrigation, then cod-liver oil employed for the next five months, with re-expansion of the left lung. The fluid became free from bacilli after use of cod-liver oil, with gradual expansion of the lung. Pneumothorax was instituted and continued on the right lung for ten months, when the patient had a spontaneous pneumothorax. It was then discontinued. Fig. 1*B* (taken Dec. 30, 1943) shows lesions in both lungs well healed. Sputum was negative for tubercle bacilli four years after both lungs re-expanded. If the patient's left lung had not re-expanded, a thoracoplasty would have been inevitable and the patient's life jeopardized by the spontaneous pneumothorax which occurred in the opposite lung.

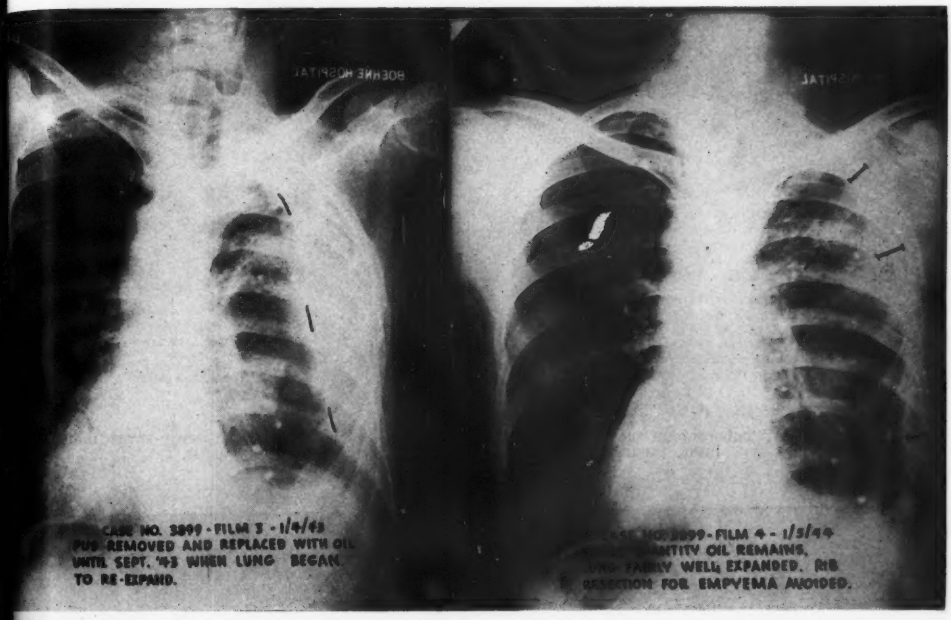

CASE NO. 01914 - EMORY - FILM X - FEB. '39
PNEUMOTHORAX INSTITUTED ON THE RIGHT. LESION MARKEDLY CLEAR AFTER 8 MOS. TREATMENT. PYOPNEUMOTHORAX, LEFT, CONTROLLED BY COD LIVER OIL.
CASE NO. 01914 - FILM X - 12/30/43
AFTER 10 MOS. TREATMENT WITH AZOCHLORAMID 1-3300 AND 5 MOS. COD LIVER OIL, LEFT LUNG RE-EXPANDED. PNEUMO. ON RT. DISCONTINUED AT 10 MOS. AFTER SPONTANEOUS PNEUMO. GASTRICS NEGATIVE FOR TB. 4 YRS.

A. *B.*

Fig. 1.—*A*, Tuberculous empyema, left, of ten months' duration; pneumothorax right. *B*, Four years later, lesions in both lungs well healed. Left lung re-expanded after five months' treatment with oil.

Case 2.—This patient had infiltration with cavitation in the right upper lobe and infiltration in the left upper lobe, with probable cavitation in the left midzone. The sputum was positive. The patient was on a bed rest regime for sixteen months. Pneumothorax was instituted on the right side in July, 1939. Fluid formed in December, 1940, and pus in 1941. The pleural cavity was aspirated and irrigated with azochloramid 1:3300 until December, 1941, at which time peanut oil was instilled. There was no clinical reaction. Fig. 2*A* (taken Jan. 4, 1943) demonstrates the pleural cavity filled with oil. During 1942 and 1943 the patient had pus and oil removed, approximately once a month. A total of 2,000 c.c. of oil

was instilled to maintain complete filling, since some of the oil was removed with each aspiration. The mixed infection disappeared three months after oil was instilled. In November, 1942, about eleven months after oil instillation, tubercle bacilli disappeared. The lung did not begin to re-expand until ten months later (September, 1943). Fig. 2*B* (taken Jan. 5, 1944) shows the lung fairly well re-expanded, with a small quantity of oil and fluid present. The lesions in the parenchyma are apparently well healed. Sputum is negative for tubercle bacilli. The earlier use of oil will tend to eliminate this type of case, as well as that of Case 1.

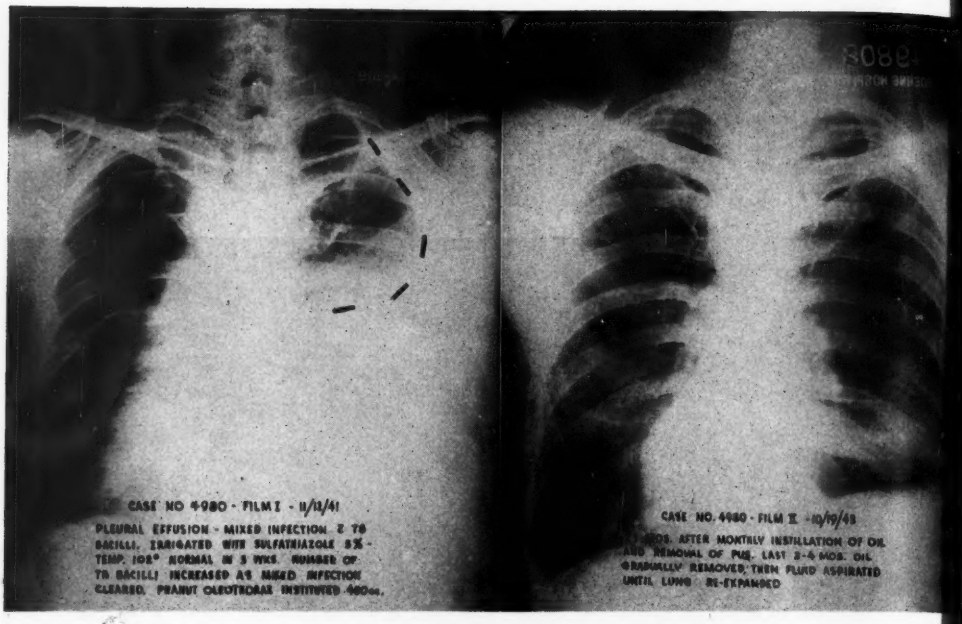

CASE NO. 3899 - FILM 3 - 1/4/43
PUS REMOVED AND REPLACED WITH OIL
UNTIL SEPT. '43 WHEN LUNG BEGAN
TO RE-EXPAND.
FILM 4 - 1/5/44
QUANTITY OIL REMAINS.
LUNG FAIRLY WELL EXPANDED. RIB
RESECTION FOR EMPYEMA AVOIDED.

A. *B.*

Fig. 2.—*A*, Tuberculous empyema; pus replaced with oil. *B*, Lung nearly re-expanded after three years' treatment with oil.

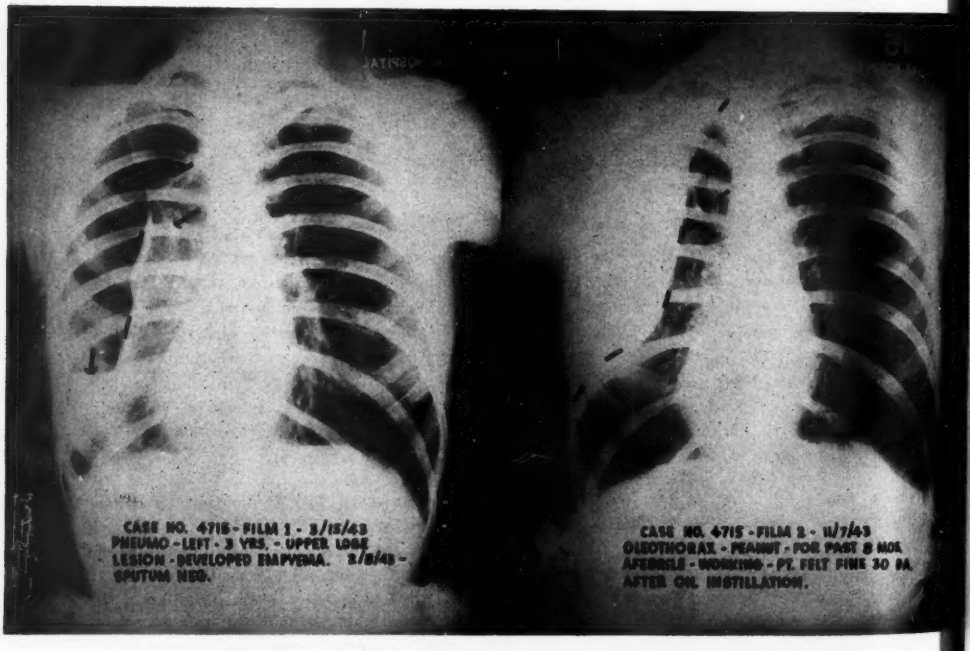
Case 3.—In November, 1941, this patient had a pleural effusion with a mixed infection, in addition to tubercle bacilli. The cavity was irrigated for two weeks with a 5 per cent sulfathiazole solution. A temperature of 102° F. returned to normal in three weeks. Fig. 3*A* (taken Nov. 12, 1941) demonstrates the extent of the pleural effusion, which was quite purulent. The number of tubercle bacilli increased as the mixed infection cleared. Peanut oleothorax was then instituted. Pus was removed periodically, every two weeks in the beginning and then every month for eight months. During the last three or four months, when the space was small, clear fluid was aspirated, which assisted the re-expansion of the lung. Fig. 3*B* shows the lung after re-expansion following treatment over twenty-three months. The patient was able to work during eighteen months of this lengthy treatment.

Case 4.—The left upper lobe of this patient was involved with infiltration. Pneumothorax was instituted in December, 1940. After a satisfactory collapse, sputum became negative. In March, 1943, fluid developed (Fig. 4*A*, taken March 15, 1943) and tubercle bacilli were present. A preliminary instillation of 50 c.c. of peanut oil was made, followed by 500 c.c. Later another 100 c.c. of oil was added. Thirty days after initial instillation the patient started to gain weight, became free from toxic symptoms, and was able to return to work. Subsequent examinations of the pleural cavity content showed no increase in accumulation of fluid. Tubercle bacilli disappeared from the fluid six months after instillation of oil. Lung is re-expanding gradually and at the present time oil is being removed periodically. Fig. 4*B* (taken Nov. 7, 1943) shows the oleothorax eight months after its establishment. Arrow points to parenchymal lesion, which is well fibrosed.


CASE NO 4980 - FILM I - 11/13/41
PLEURAL EFFUSION - MIXED INFECTION. + TB BACILLI. IRRIGATED WITH SULFATHIAZOLE 5% - TEMP. 102° NORMAL IN 3 WKS. NUMBER OF TB BACILLI INCREASED AS MIXED INFECTION CLEARED. PEANUT OLEOTHORAX INSTITUTED 400cc.
CASE NO. 4980 - FILM II - 10/19/43
MOS. AFTER MONTHLY INSTILLATION OF OIL AND REMOVAL OF PUS. LAST 2-4 MOS. OIL GRADUALLY REMOVED; THEN FLUID ASPIRATED UNTIL LUNG RE-EXPANDED

A. *B.*

Fig. 3.—*A*, Tuberculous pleural effusion replaced with oleothorax. *B*, Twenty-three months later, pleural surfaces approximated by obliterative pleuritis.


CASE NO. 4715 - FILM 1 - 3/15/43
PNEUMO - LEFT - 3 YRS. - UPPER LOBE LESION - DEVELOPED EMPYEMA. 2/8/43 - SPUTUM NEG.
CASE NO. 4715 - FILM 2 - 11/7/43
OLEOTHORAX - PEANUT - FOR PAST 8 MOS. AFEBRILE - WORKING - PT. FELT FINE 30 PA. AFTER OIL INSTILLATION.

A. *B.*

Fig. 4.—*A*, Pus removed from pleural space prior to instillation of oil. *B*, After an oleothorax of eight months' duration, pleural content was negative for tubercle bacilli. Oil can now be removed gradually.

CASE 5.—Pneumothorax had been instituted sixteen months prior to the taking of this radiograph (Fig. 5*A*, taken April 5, 1944). Fluid was discovered seven months later. Negative pressure was maintained and aspirations were carried on until August, 1943, when tubercle bacilli were discovered. Peanut oleothorax was instituted. This was checked frequently during the first month for any increased accumulation of fluid. In November, 1943, 100 c.c. were aspirated and in April, 1944, 150 c.c. This increase indicates the rate of accumulation of fluid in this particular patient. No tubercle bacilli were found in either specimen. The oleothorax was continued because of the parenchymal lesion which had not been collapsed for a sufficient length of time.

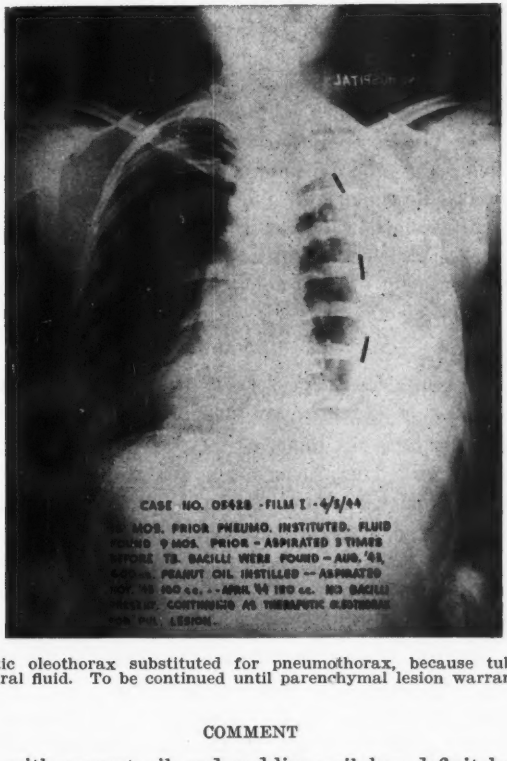


Fig. 5.—Therapeutic oleothorax substituted for pneumothorax, because tubercle bacilli persisted in the pleural fluid. To be continued until parenchymal lesion warrants re-expansion.

COMMENT

Oleothorax with peanut oil and cod-liver oil has definitely established its value in controlling tuberculous infection of the pleurae. Further treatment of the empyema space is determined by the condition of the lung. We have found that an oleothorax of irritant oils produces an obliterative pleuritis and seals over the subpleural foci of infection. If the visceral pleura is not too thick and the lung shows a tendency to re-expand, an uncontrolled infection in the lung can be given priority and the oleothorax continued. When the parenchymal lesion is healed, the lung may be allowed to re-expand. The lung gradually re-expands, if assisted by periodic removal of oil and air if present, with maintenance of negative intrapleural pressures. If the lung does not re-expand entirely, a less extensive thoracoplasty than would otherwise be necessary can be performed. This early use of irritant oils may ban the mutilating Schede procedure.

In the conduct of oleothorax, frequent examination of the patient with periodic removal of pus or fluid, and maintenance of negative intrapleural pressures, is mandatory. This avoids empyema or oleum necessitans through

a needle opening, and diminishes the chances for the formation of a bronchial fistula. There is great individual variation in the rate of fluid or pus formation and disappearance of tubercle bacilli. Oil and a little fluid, with or without bacilli, can be present in the chest for an indefinite period without clinical symptoms. One patient with diabetes, a very poor surgical risk, who had a tuberculous empyema, carried cod-liver oil and pus in the pleural space for six years before a bronchial fistula developed. This patient failed to report for aspirations during this time and increased tension helped to cause the fistula. With oleothorax, the surgical problems of aspiration are diminished, and closed drainage with empyema tubes and catheters eliminated. We have always considered open drainage contraindicated, unless a bronchial or pleural fistula is present. Of twenty patients, with varying degrees of purulent effusion and empyema, six have experienced re-expansion of the lungs without reactivation of the pulmonary infection or further plastic operation for closure of the pleural space. Of the remaining fourteen patients, ten now have oleothoraces which are negative for tubercle bacilli. Re-expansion of a lung may be lifesaving to the patient if a tuberculous infection develops or is present in the other lung, as it was in eleven cases of this series. The use of irritant oils in oleothorax adds a reversible procedure to the treatment of tuberculous empyema, which heretofore has often demanded an irreversible one.

SUMMARY

1. Tuberculous empyema is a formidable complication of pneumothorax therapy and presents both immediate and late surgical problems.

2. The use of irritant oils in oleothorax, such as peanut oil and cod-liver oil, brings about a marked improvement in the clinical picture of the patient by reducing the toxic effects of the tuberculous infection.

3. An irritant oil not only inhibits the growth of the tubercle bacillus by physical action,[6] but it stimulates the production of exudate, which seals over the focus of infection in the lung. Therefore, it is not primarily a disinfection pneumothorax.

4. Periodic removal of pus and instillation of oil to fill the entire pleural cavity lessens the chances of spreading the infection.

5. An irritant oil aids in the formation of an obliterative pleuritis which re-expands the lung. Re-expansion of the lung, which avoids thoracoplasty or limits its extent, is advantageous to the patient if a tuberculous infection develops in the contralateral lung.

6. The use of irritant oils in oleothorax adds a reversible procedure to the treatment of tuberculous empyema, which often demands an irreversible one.

7. Of twenty patients with tuberculous empyema undergoing treatment, six up to date have had re-expansion of the lung without requiring thoracoplasty for either the empyema cavity or the infected lung. Of the remaining fourteen patients, ten now have oleothoraces which are negative for tubercle bacilli.

The cod-liver oil used in this study was furnished by Mead Johnson & Co., Evansville, Ind., and the peanut oil by Magnus, Mabee, and Reynard, Inc., New York, N. Y.

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DISCUSSION

DR. JEROME R. HEAD, CHICAGO, ILL.—The results that Dr. Crimm has shown in his x-rays have been very interesting. I had always felt that oleothorax was more or less of a permanent procedure and was not as reversible as he has shown it to be in a good many cases. Our procedure in treating tuberculous empyemas is to irrigate them daily with azochloramid solution through a needle. We have been able in practically every case to change the purulent fluid into serous fluid and then into no fluid and finally to re-expand the lung or continue the collapse.

I would like to report one case that I still do not understand. A young woman who had an oleothorax for eight years developed a high fever and a severe cough. She came in a few days later and was found to have evacuated all of the oil. She had a pneumothorax instead of the oleothorax. I expected to have to drain her chest and do a thoracoplasty. She had no secondary infection. The fistula closed and she is now being treated by pneumothorax.

DR. PAUL D. CRIMM, EVANSVILLE, IND.—In reply to Dr. Head's discussion, we find that the use of an irrigating solution in a tuberculous empyema is a waste of time and material as far as disinfecting the tubercle bacillis is concerned. An irritant oil like cod-liver oil or peanut oil stimulates a pleuritis which obliterates the pleural space. If it is possible to obtain a pleuritis with azochloramid it is quite satisfactory, but we have been unable to accomplish this result with any chemical.

BENIGN TUMORS OF THE ESOPHAGUS

REPORT OF THREE CASES

RALPH ADAMS, M.D.,* AND WALTER B. HOOVER, M.D.† (BY INVITATION)
BOSTON, MASS.

REVIEW OF LITERATURE

BENIGN tumor of the esophagus is a rare disease, whether considered in terms of the total number of reported cases, the frequency in respect to all esophageal tumors, or the percentage of all patients with esophageal symptoms in whom the cause is a benign tumor. However, these lesions comprise an important clinical group because they are readily curable by proper surgical management. They are interesting from the standpoint of differential diagnosis, prognosis, and rarity, and are a challenge to the surgeon who finds pleasure in detecting and correcting the bizarre ailment.

Patterson,[14] who published reviews of this subject in 1932 and 1933, was able to find only 62 cases reported between 1712 and 1932. Many of these were incidental discoveries at autopsy. Upon reviewing the literature for the succeeding eleven years, 1933 to 1943, we found 26 additional cases[1-13, 15-23] and are adding 3 of our own, making 29, for a total of 91 cases. Dr. S. W. Harrington of the Mayo Clinic, at the May, 1944, meeting of the American Association for Thoracic Surgery, reported 6 more cases, with mention of a seventh previously reported by Moersch and Broders.[13] The grand total known to us is, therefore,

Read (by title) at the Twenty-Fifth Annual Meeting of the American Association for Thoracic Surgery, Chicago, Ill., May 5 and 6, 1944.

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†Department of Ear, Nose and Throat, The Lahey Clinic.

97 cases. As the details of these last 6 cases had not been published when this article was written, they are not included in our tabulation.

During 1933 to 1943, the percentage of cases diagnosed during life was higher, which is explained by the increasingly widespread use of the precision methods of diagnosis—fluoroscopy with barium and esophagoscopy. Also, the number of cases discovered and recorded during the last eleven years is over one-half as large as the number of cases reported in the preceding 220 years.

Although the benignity, location, and type of attachment are matters of greater practical concern than the pathologic subclassification, the data of 91 cases allow deductions sufficiently reliable to appease curiosity about the relative frequency of the various benign lesions. The distribution is shown in Table I.

TABLE I

PATHOLOGICAL DIAGNOSIS	NUMBER		TOTAL
	1712-1932	1933-1943	
Aberrant thyroid	1		1
Adenoma	2	1	3
Benign giant-cell tumor		1	1
Cyst	4	2	6
Fibroma	2	5	8
Hemangioma	1		1
Leiomyoma	6		6
Lipoma	2	3	5
Lipomyoma	1		1
Myoma	8	2	10
Myxofibroma	1		
Neurofibroma		1	1
Osteochondroma		1	1
Papilloma	8	1	9
Polyps	26	9	35
Unclassified benign tumor		3	3
Total	62	29	91

The bibliography is believed to be complete, but mathematical accuracy in the compilation is not implied because the limitations of war make it impossible to obtain certain foreign journals in which isolated cases are reported or to correspond with the authors. The articles apparently reporting benign esophageal tumors, but unavailable to us for review, are listed separately in the references.[24-32] These cases are not included in Table I.

REPORT OF CASES

Three patients have been referred for treatment during the last three years.

CASE 1.—A woman, aged 48 years, entered the clinic March 3, 1941,[11] complaining of substernal pressure, persistent dry cough, orthopnea and dyspnea on exertion, and recent rasping breathing. No difficulty in swallowing had occurred.

Fluoroscopy with barium and roentgenograms demonstrated a soft tissue mass lying in the low cervical region, displacing the lumen of the barium-filled esophagus forward (Fig. 1). In the corresponding region there was anteroposterior narrowing of the tracheal lumen. The mass ascended and descended with swallowing. The mucosa of the esophagus appeared intact. The differential diagnosis was thought to include tumor of the esophageal wall and intrathoracic goiter, and operation was advised.

The mass was exposed, March 7, through a transverse collar-type incision, as customarily employed for subtotal thyroidectomy. It lay in the lower cervical mediastinum near the inferior pole of the right thyroid lobe alongside the esophagus and immediately posterior and slightly to the right of the trachea. Both the recurrent laryngeal nerve and the inferior thyroid artery were anterior to the tumor.

After ligation and division of the inferior thyroid artery, the tumor mass was exposed further and found to be covered in part by longitudinal muscle fibers of the esophageal wall. These fibers were split longitudinally down to the capsule of the firm, fibrous tumor mass,

which then was rotated laterally and anteriorly to the recurrent nerve, thus exposing the pedicle of the growth and the mucosa of the esophagus. Removal was completed by ligation and division of the pedicle; the esophageal muscle fibers were reapproximated; a cigarette drain was inserted down to the mediastinum and the wound closed.

The drain was removed on the sixth postoperative day, and after an uneventful convalescence she was discharged March 20, the thirteenth postoperative day. A follow-up report four months later indicated that she was symptom free. The pathologic report was fibroma.

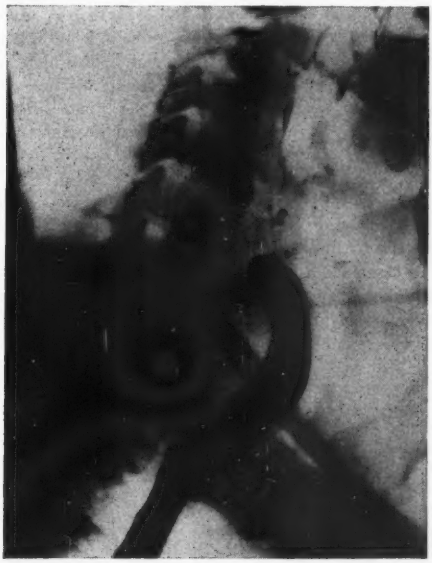


Fig. 1.—Distortion of esophagus caused by intramural fibroma.

CASE 2.—A woman, aged 41 years, entered the clinic, June 18, 1942,[1] complaining of difficulty in swallowing, of seven years' duration.

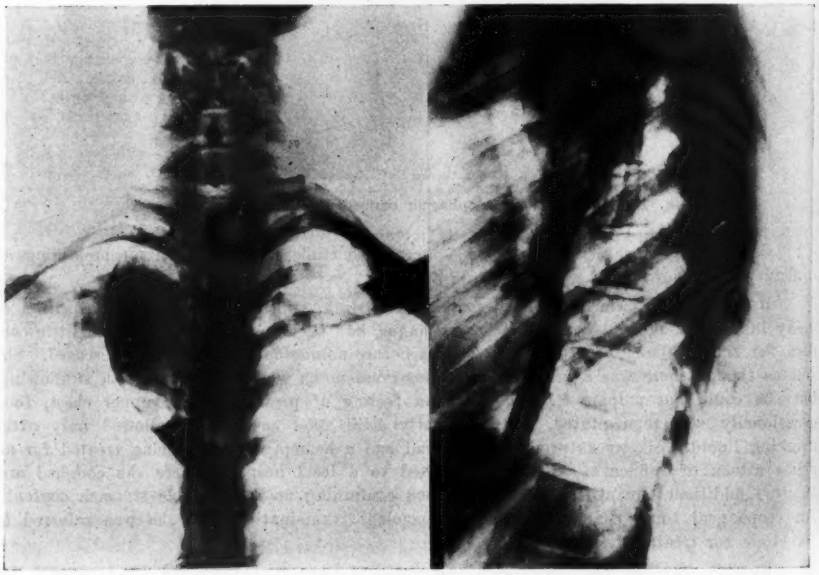
Her symptoms, which consisted mainly of a slight substernal ache and a sensation of delay in the passage of food down the esophagus, had been vague and had caused little concern for six and one-half years. Six months before admission the symptoms increased. She felt as though there was a lump in the suprasternal notch which interfered with swallowing, but she could not palpate it. There was a feeling of pressure in the upper chest, food occasionally was regurgitated, and frequently solid food could be swallowed only after drinking liquid. Six weeks previously she had had a hemoptysis while being treated for an acute attack of influenza. She was admitted to a local hospital where she coughed and vomited additional quantities of clotted blood containing no recognizable stomach contents. An esophageal tumor was found on roentgenologic examination, and she was referred to the clinic for treatment.

Routine physical and laboratory examinations were within normal limits except for nodular thickening in the pouch of Douglas characteristic of endometriosis. Fluoroscopy with barium outlined a 5 by 7 cm. mass in the upper thoracic esophagus, above which the lumen was dilated. The mucosal relief pattern was intact where outlined by the barium, and was visualized everywhere except along the right posterolateral wall where the barium did not pass. The excellent roentgenograms of the lesion (Figs. 2 and 3), which the patient brought with her, were made under the supervision of Dr. George A. Green, Mechanicville, N. Y.

Esophagoscopy revealed a large, globular, smooth-surfaced mass in the upper thoracic esophagus with an attachment on the right posterolateral wall. There was superficial inflammation of the mucosa above the tumor and there was a small ulceration on the upper surface of the growth. Mucosa passed from the pedicle out onto a portion of the mass and then disappeared. The gross appearance was that of a benign lesion and a biopsy specimen was not taken.

A simple catheter gastrostomy was established on June 19, and on July 8 the right pleural cavity was opened widely through a long subscapular incision and the bed of the third rib. The right lung was allowed to collapse and the esophageal mass became immediately evident as it lay in the posterior mediastinum at the level of the third thoracic vertebra. The posterior parietal pleura over the mass was incised and retracted. The thin muscularis was divided longitudinally, and it was then evident that the mass lay entirely within the esophagus rather than arising extramucosally in the muscular layers and extending into the lumen.

After the esophageal mucosa was opened at the lower border of the tumor, the mass was drawn out of the lumen. The pedicle, which was 1 cm. in length, consisted of a cylindrical strand of soft tissue covered by mucosa. It left the right posterolateral wall of the esophagus and spread out over the upper margin, rapidly becoming thinner until it disappeared into the hard, pearly gray, slightly nodular surface of the tumor itself. A small ulceration, 5 mm. in diameter, lay just at the junction of recognizable mucosa with the tumor surface proper. The blood supply was minimal; the tiny vessels within the pedicle were surrounded by scanty areolar tissue. The pedicle was ligated and divided at the base and the cut surface enfolded with adjacent normal mucosa by means of two interrupted fine silk mattress sutures. The longitudinal opening in the esophagus was closed in three layers, using extremely fine silk carried on tiny curved needles as interrupted sutures for each layer. The knots approximating the mucosa were tied within the esophageal lumen and those approximating the muscularis were tied outside the muscular layer. The parietal pleura formed the third layer. After 4 Gm. of sulfanilamide powder were placed in the mediastinum about the esophagus, the lung was re-expanded and the pleural cavity was closed without drainage.



Figs. 2 and 3.—Esophageal changes associated with pedunculated intraluminal fibroma.

An indwelling Levin tube lying at the level of the second thoracic vertebra was kept on suction for fourteen days. During this period the patient was allowed to drink sterile water as desired but nothing else, the nutrition and principal fluid requirements being maintained by gastrostomy feeding. The oral intake was rapidly increased, after removal of the tube on the fourteenth day, until she was taking a normal diet on the twenty-first day. The gastrostomy tube was removed, the sinus closed promptly, and on August 5, twenty-eight days after operation, she was discharged fully ambulatory without dietary restrictions. Convalescence was uneventful. The pathologic report was fibroma of the esophagus.

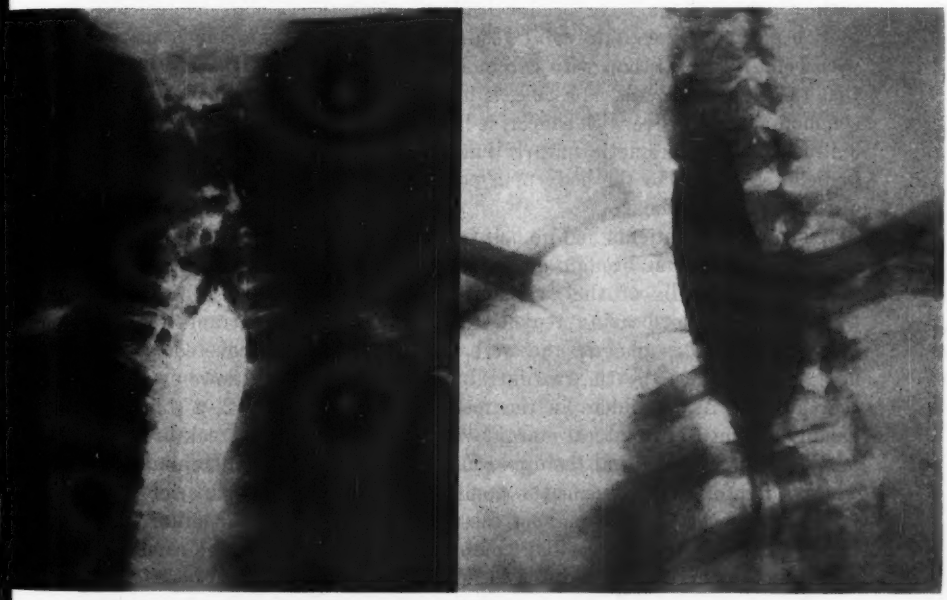
She returned to work and had no further esophageal symptoms. However, about one year after operation she re-entered the hospital with a small abscess in the upper end of the chest wall wound which had caused soreness for three weeks. A diagnosis of tuberculosis was

made on examination of debris removed from the abscess cavity. A comparison of new roentgenograms with those taken previously showed that the minimal fibrotic changes at both apices had become complicated by an exudative reaction. Sanatorium care was recommended.

CASE 3.—A man, aged 42 years, entered the clinic Nov. 30, 1942, with a complaint of intermittent difficulty in swallowing, of three years' duration. He had had an occasional sensation, when eating, of a bolus of food caught in the upper esophagus. After momentary difficulty with swallowing the sensation would disappear and he would have no further trouble for variable periods.

The incident which caused him to seek medical assistance is of both scientific and human interest. About four months previously, while attending a reception where oysters were served, he suddenly coughed and felt as though he were being choked. After trying unsuccessfully to swallow the "oyster" in the back of his throat, he inserted his finger to remove it and found that it was impossible to do so. He next forced the mass down his throat and obtained temporary relief. Within an hour or so, however, he developed great difficulty in swallowing saliva, increasing respiratory distress, and some cyanosis. These symptoms subsided within a few days.

Esophagoscopic and roentgenologic studies at the Massachusetts General Hospital established a diagnosis of polyp of the esophagus with recent edema and hemorrhage (Figs. 4 and 5). Dr. Edward D. Churchill referred the patient to us.



Figs. 4 and 5.—Roentgenographic appearance of a pedunculated polyp in the upper esophagus. (Courtesy of Dr. Richard Schatzki.)

Physical and laboratory examinations were within normal limits. It was apparent from comparison of our esophagoscopic findings with those of Dr. Edward Benedict and roentgenograms from the Massachusetts General Hospital that shrinkage of the size of the tumor had occurred between September and November. Therefore, an attempt at endoscopic removal before resorting to an external surgical approach seemed justified.

December 2, a 22 cm. esophageal speculum was used to visualize the upper end of the esophagus. A pedunculated tumor 6.5 cm. long was hanging into the esophagus from a point of origin at the cricopharyngeus muscle. The tumor was rather translucent with several blood vessels visible along its surface. It was freely movable to-and-fro on its pedicle. It was grasped with forceps and brought upward into the speculum and the speculum was gradually withdrawn, thus delivering the tumor into the oral cavity. A suspension laryngoscope was then placed. A No. 7 endotracheal catheter was inserted to prevent difficulty from

respiratory embarrassment. The tumor was then threaded through a snare, and the loop of the snare was closed about the pedicle. Electrocoagulation was applied to the snare, coagulating through the pedicle of the tumor as it was slowly divided. A Levin tube was passed through the esophagus into the stomach for feeding purposes.

The patient pulled the tube out on the following day and since we hesitated to reinsert it, fluid and electrolyte balance were maintained by intravenous administration for seven days. He then rapidly resumed a normal peroral diet.

The pathologic report was polyp of the esophagus.

The postoperative course was uneventful except for soreness in the throat and difficulty in swallowing for a few days. He was discharged December 21, the twelfth postoperative day. He had no further symptoms and checkup examinations, Jan. 11, 1943, with fluoroscopy and thick and thin barium in the esophagus showed no delay or recognizable esophageal defect.

DISCUSSION

The symptoms of all esophageal lesions are so similar that they usually afford little differential diagnostic information. A small tumor rarely causes any symptoms and unless discovered incidentally in the course of fluoroscopic examination, its presence ordinarily is not suspected until its size interferes with swallowing. In reviewing our cases of carcinoma of the esophagus and the literature of benign esophageal tumors, one is impressed with the frequency with which patients have been considered neurotic (globus hystericus) until they began to regurgitate solid food. Dysphagia appears much more slowly with benign tumors than with carcinoma. This is partly explained by the facts that the rate of growth, as a rule, is much less rapid, and that ulceration, while common and extensive with cancer, is late and minimal with benign tumor. Case 3 illustrates the dramatic nature that symptoms may assume if torsion of the pedicle or trauma to the body of a pedunculated benign tumor induces venous obstruction and edema.

These three patients had no helpful physical signs, but in all, roentgenologic studies with barium brought out characteristic features of benign esophageal tumors. The walls of the esophagus appear elastic. Peristaltic waves pass through the tumor-bearing region. Even with a large intramural growth in one wall of the esophagus, the wall directly opposite is covered with normal mucosa. As shown by the two intraluminal cases, barium flows evenly around the tumors. As is evident in the roentgenograms in Case 2, a thin stream of barium outlined each lateral margin of the growth with no break in the regular mucosal pattern, except at the upper margin of the negative intraluminal shadow where a film of barium seemed to be fitted as a cap over the superior tumor surface. One needs only to compare these roentgenograms with similar ones showing the narrow, thick, irregular channel of a carcinoma in the same region to realize how definitely they differ in appearance.

The first patient had no esophagoscopic examination because neither the symptoms nor the roentgenographic examination indicated an intraluminal lesion. The fact that this tumor ascended and descended with swallowing made intrathoracic goiter by far the most likely preoperative diagnosis on a purely statistical basis, because in point of frequency intrathoracic goiter outnumbers all other diagnoses combined for tumors of the superior mediastinum which move with deglutition. Lesions attached to the wall of the cervical esophagus are about the only other possibility. The demonstration of a tumor in the neck or mediastinum posterior to the recurrent laryngeal nerve excludes goiter from consideration, in our experience, because in over 23,000 thyroid operations we have never seen a goiter descend into the mediastinum posterior to the nerve. Furthermore, the displacement shown by roentgenogram of the esophagus and trachea is out of proportion to that expected from asymmetrical, nodular goiters.

Finally, its solid consistency and esophageal muscle covering excluded diverticulum and established tumor of the esophageal wall as the only tenable diagnosis in the mind of the operator.[11] The problem was reduced to the purely technical one of removing the tumor from the wall of the esophagus without perforation of the mucosa, and this was successfully accomplished.

At esophagoscopy in Case 2, the temptation to take a biopsy specimen was resisted because the tumor looked benign. This is important,[1] whether considering an intramural tumor covered by intact mucosa or an intraluminal tumor, if surgical removal is shortly to be attempted, in order to minimize the risk of perforation and infection, or spreading lymphatic infection. When a pedunculated intraluminal tumor has been shown by roentgenogram to be probably benign and possibly removable by endoscopic methods, it seems wise to have facilities available for proceeding with removal at the time of the initial esophagoscopy. Otherwise the mucosal irritation attendant upon the examination may set up superficial esophagitis which persists for some time in the presence of partial obstruction, and manipulation of the tumor may cause sufficient edema of the pedicle to induce tumor necrosis or infection with increased swelling, obstruction, and the various conceivable complications.

The extirpation of each of these lesions presented some problems peculiar to location, pathology, and the anatomy of the esophagus. In Case 1 we had to determine with certainty from which organ the tumor arose and, having localized it to the wall of the esophagus, remove it with preservation of an intact mucosa. In Case 3, an easy and safe endoscopic operation instead of a hazardous external operation through the incised cervical esophagus depended upon the suspension laryngoscope for good exposure and upon the electrocoagulating snare for reliable hemostasis.

In Case 2, the problem was somewhat more involved. The tumor was too large to be removed endoscopically. It was situated too low to be reached through an incision in the neck. Yet such a tumor must be removed with maintenance of esophageal continuity, or one must accept the alternative of an esophageal resection, cervical esophageal fistula, gastrostomy and external esophagoplasty with the multiple operations, mutilation, and frequent disappointment. In order to avoid fatal postoperative mediastinitis, rigid asepsis and perfect healing must be achieved. As a contribution to attainment of these ideals, the esophagus should be defunctioned during the periods of preoperative esophageal sterilization and postoperative healing. Finally, one must be able to operate in the upper posterior mediastinum, a region admittedly difficult of surgical access, with the wide exposure prerequisite to painstaking and aseptic technique.

A posterolateral thoracoplasty type of incision with removal of the third rib permitted wide exposure of the tumor and direct approach to the pedicle. Crushing clamps and forceps were carefully avoided during the operation because of the ease with which esophageal tissue may be traumatized and the blood supply jeopardized by manipulation. The edges of a short linear incision in the esophageal wall over the tumor were held apart with silk traction sutures, and an additional traction suture placed in the apex of the tumor permitted its delivery into a carefully protected field without touching it or the esophageal mucosa with the hands or clamps. Extremely fine sutures were used for closure to avoid trauma. The knots were tied internally for the mucosa and externally for the muscularis to minimize foreign body reaction, and the sulfonamides were, of course, used locally and systemically for bacteriostatic effect. Perhaps

this extreme attention to the minutiae of technique, even in its apparently insignificant details, was more rigorous than necessary. Certainly, it was time consuming, but we greatly feared mediastinitis from operative infection or later leakage of the suture line. Therefore, we do not know whether the primary healing is attributable to proper technique or good chemotherapy.

SUMMARY

The literature of benign tumors of the esophagus is reviewed. Three cases are reported. Various diagnostic and technical problems arising in the management of such cases are discussed.

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RELAXING THORACOPLASTY

Preliminary Report

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IN THE treatment of pulmonary tuberculosis, prevention of the disease is the ultimate goal. On the other hand, if all patients could be treated when the disease is minimal, major thoracic operations for the arrest of the disease would not be necessary. However, patients must be treated for the disease as they present themselves. All those suffering from pulmonary tuberculosis are not suitable candidates for the modern extrapleural thoracoplasty, particularly the patient whose disease is bilateral, the one with a tension cavity, and the patient with some other concomitant disease. Many patients have tuberculous pulmonary lesions which seemingly do not warrant an operative procedure of the magnitude of a standard thoracoplasty. For these particular types of patients and with the ever-present desire to improve even the seemingly satisfactory results from the standard thoracoplasty, a modified type of thoracoplasty has been tried.

Under the influence of the teachings of Forlanini, and working with Morelli,[19] the physiology of chest movements was described by Monaldi.[18] He defined the behavior of the four dominants, a superior vertical regulated by the muscles of the superior thoracic aperture and an inferior vertical regulated by the diaphragm. Two dominant lines of motion occurred in the thorax, one postero-anterior and the other transverse-lateral following a line beginning at the first interspace at the sternum and going obliquely outward to the mid-axillary line at the seventh interspace. By interrupting the muscles of the superior aperture, paralyzing the diaphragm, and doing costectomies along the dominant line, the chest was made static and the lung was freed from respiratory trauma. Under the direction of Alessandri the operative procedure was systematized by Ascoli.[19] It has gone through various modifications[2] and has been reported upon favorably by all those interested in its conception,[3] and by Katyar,[13, 14] who studied with them. Finochietto and Aguilar,[12] as well as Chiariello,[10] reviewed the procedure and felt with certain limitations it might fill a need in the treatment of some patients with pulmonary tuberculosis. The method was tried by Maurer and Rautureau[17] in four patients, all of whom showed poor results. They criticized the procedure and then decided to modify the operative technique.

The dominant lines of stress and motion as described by Monaldi seem accurate but more than pulmonary rest is necessary to heal many cases of pulmonary tuberculosis.

In pulmonary tuberculosis there is considerable evidence to support the view that one must consider the condition of the bronchial tree[8, 9] as well as the type of parenchymal disease. Three general types of bronchial conditions can be recognized. In one type this condition leads to increased intrapulmonary

From Maryland State Tuberculosis Sanatorium, Mount Wilson Branch, Mount Wilson.
Read (by title) at the twenty-fifth annual meeting of the American Association for Thoracic Surgery, Chicago, Ill., May 5 and 6, 1944.

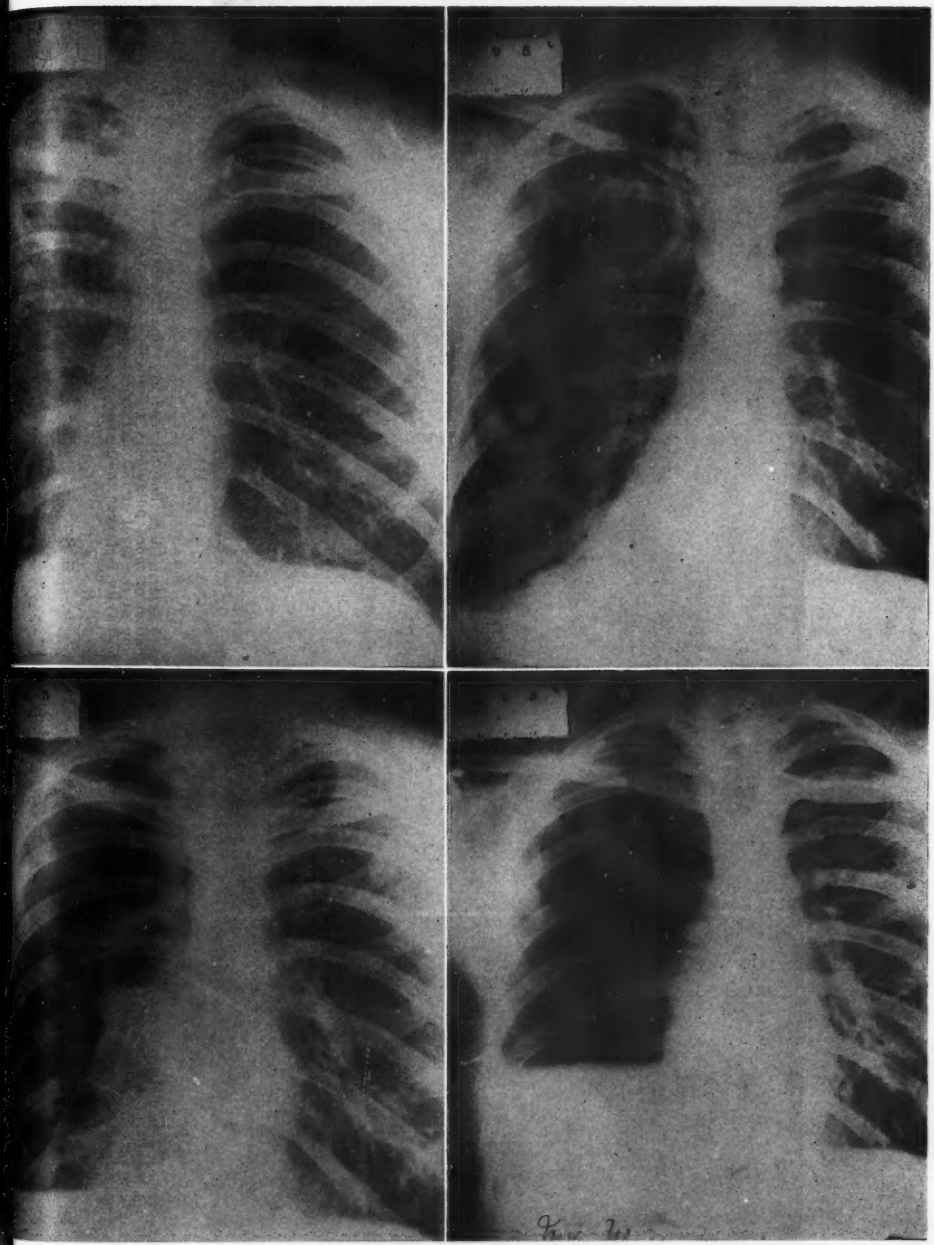
pressure or increased pressure within the tuberculous lesion.[21] It is one in which, either because of organic factors or muscular spasm involving the bronchial musculature,[15] air freely enters into the alveoli during inspiration but its escape is delayed on expiration (Fig. 5, *C* and *D*). The presence of tuberculous lesions in the bronchi or bronchioles seems to induce the spasm. Since the bronchi normally narrow on expiration[16] it is not surprising that the escape of air is impeded more than the inflow of air on inspiration, when the bronchi are largest. This accounts for the tension cavities and for rapid re-expansion of a lung after pneumonolysis.[7] When on a spasmodic basis alone, it is much like the intrapulmonic tension found in asthmatic lungs[6] without pulmonary tuberculosis. If on an organic basis, the blockage in the bronchus is a check valve mechanism which allows the free flow of air into the lung but obstructs its outflow (Fig. 1). The condition is not always permanent and there may be spontaneous relief of the tension mechanism (Fig. 2). As opposed to increased intrapulmonary pressure, a form of bronchial condition occurs which leads to a hypotensive lung. In this type the bronchus may be partially or completely occluded by organic disease or its secretions, or by decrease in the tonus of the bronchial musculature permitting only a minimal amount of air into the alveoli but allowing this air to escape easily. Actually, a check valve exists which operates in an opposite direction of the first type described (Fig. 3). Obstruction may be complete and alveolar air is removed by the normal circulation (Fig. 4). Thus, a contracting or hypotensive type of lung is produced. Many workers[4, 11, 20, 21, 23] believe bronchial occlusion is the most common method of cavity healing. In the third type the bronchi may be free of organic or spasmodic involvement. Air is permitted to flow freely in and out of the alveoli and bronchial tree. This produces a lung with normal intrapulmonary pressures. The three types need not necessarily remain as such; one may merge into the other and back again, since disease is a dynamic process and not a static one.

The static condition produced by the Monaldi operation seemed beneficial. It also appeared strikingly evident that if the thoracic cage could be relaxed when the contracting phase of bronchial disease occurred perhaps the lung could contract easily because the restraining force of a rigid thoracic cage had been removed. The same would be true if healing was taking place by scar tissue contraction. Thus, contraction would be encouraged and it would be more likely to remain until the healing was complete. The belief that a relaxed thoracic cage might be more desirable than a rigid collapsed thoracic cage is strengthened by the evidence that collapse of the lung in itself does not necessarily mean healing nor cavity closure (Figs. 5 and 6). With these principles in mind, an operative procedure was undertaken primarily for those with tension cavities and for patients with extensive disease from the apex to the base on one side but without giant cavities. The early results seemed highly encouraging and the operation was perhaps unwisely applied to patients with hopeless bilateral disease and to some with giant cavities. It also was applied to older patients and to those with concomitant disease. Unfortunately, it was not applied to patients whose pulmonary disease was of insufficient magnitude to warrant a routine standard thoracoplasty. In a few cases it was applied to those who would have been good candidates for the modern thoracoplasty.

OPERATIVE TECHNIQUE

All of the operative stages are done under local anesthesia. Procaine, 0.5 per cent, with 3 minims of 1:1000 adrenalin to the ounce is used for infiltration and

A. B.



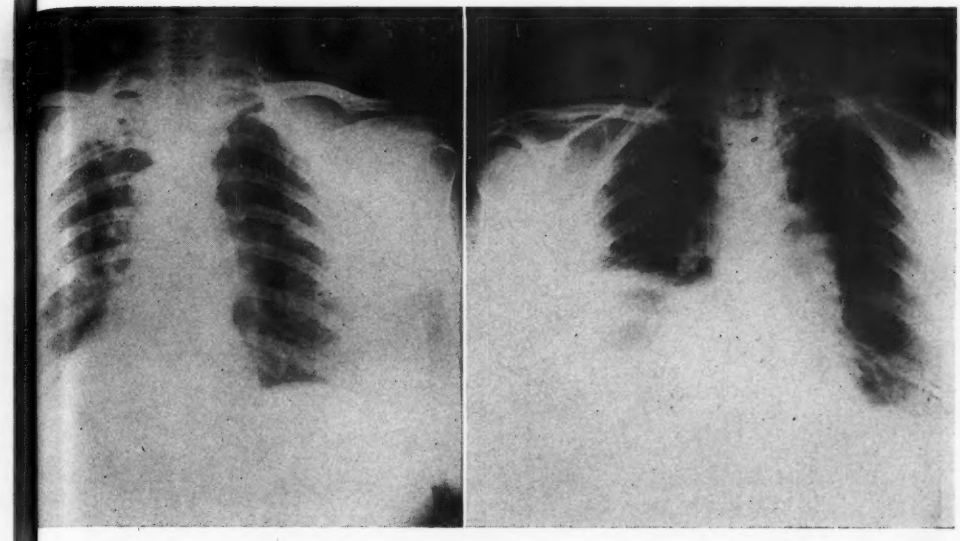
C. D.

Fig. 1.—This group of roentgenograms reveals a tension type of lesion resulting from an endobronchial tuberculous lesion which causes a check valve obstruction to the cavity. This check valve obstruction was relieved by bronchoscopic treatment.

A, Before pneumothorax was instituted. *B*, The same patient after pneumothorax was initiated. The cavity is spherical, much larger, and there is little reaction about its periphery. One can argue the cavity is held open by adhesions. *C*, The adhesions were removed by closed pneumonolysis. The lung was completely freed from the parietal pleura. The cavity is smaller but not collapsed. *D*, Twenty-four hours after the treatment of an endobronchial lesion by bronchoscopy the roentgenogram reveals the cavity completely collapsed.

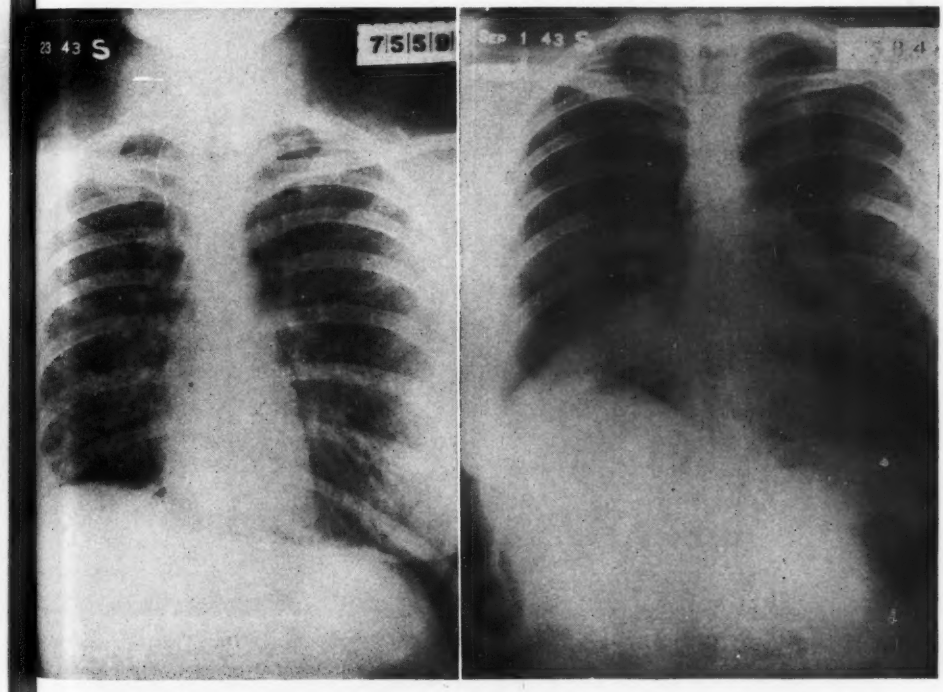
A. *B.* *C.*

Fig. 2.—This series demonstrates clearly that the condition of the bronchial system does not necessarily remain stationery. The rapid change in the cavity certainly is the result of tension and not of healing followed by the destruction of more pulmonary tissue.
A, Roentgenogram taken July 21, 1943, showing a small cavity in the left lung at the level of the sixth rib posteriorly. *B*, The same patient Aug. 4, 1943. The cavity has completely disappeared. *C*, The same patient Aug. 18, 1943. The cavity is larger than ever.



A. *B.*

Fig. 3.—*A*, Roentgenogram showing a cavity at the fourth and seventh ribs posteriorly on the left side. *B*, Temporary phrenic nerve paralysis was done. The enormous elevation of the diaphragm and prompt closure of the cavities illustrates the contracting type of lung. There was probably hypotension in the parenchyma caused by partial or complete bronchial obstruction.



A. *B.*

Fig. 4.—*A*, Roentgenogram showing tuberculous infiltration at the right base, which had not been particularly influenced by a temporary phrenic paralysis. *B*, The same patient one week later, after a pneumothorax had been induced. The area of infiltration is represented by an atelectatic lower lobe. Bronchoscopy revealed a tuberculous bronchial lesion that caused complete obstruction. This indicates a lung where hypotension exists.

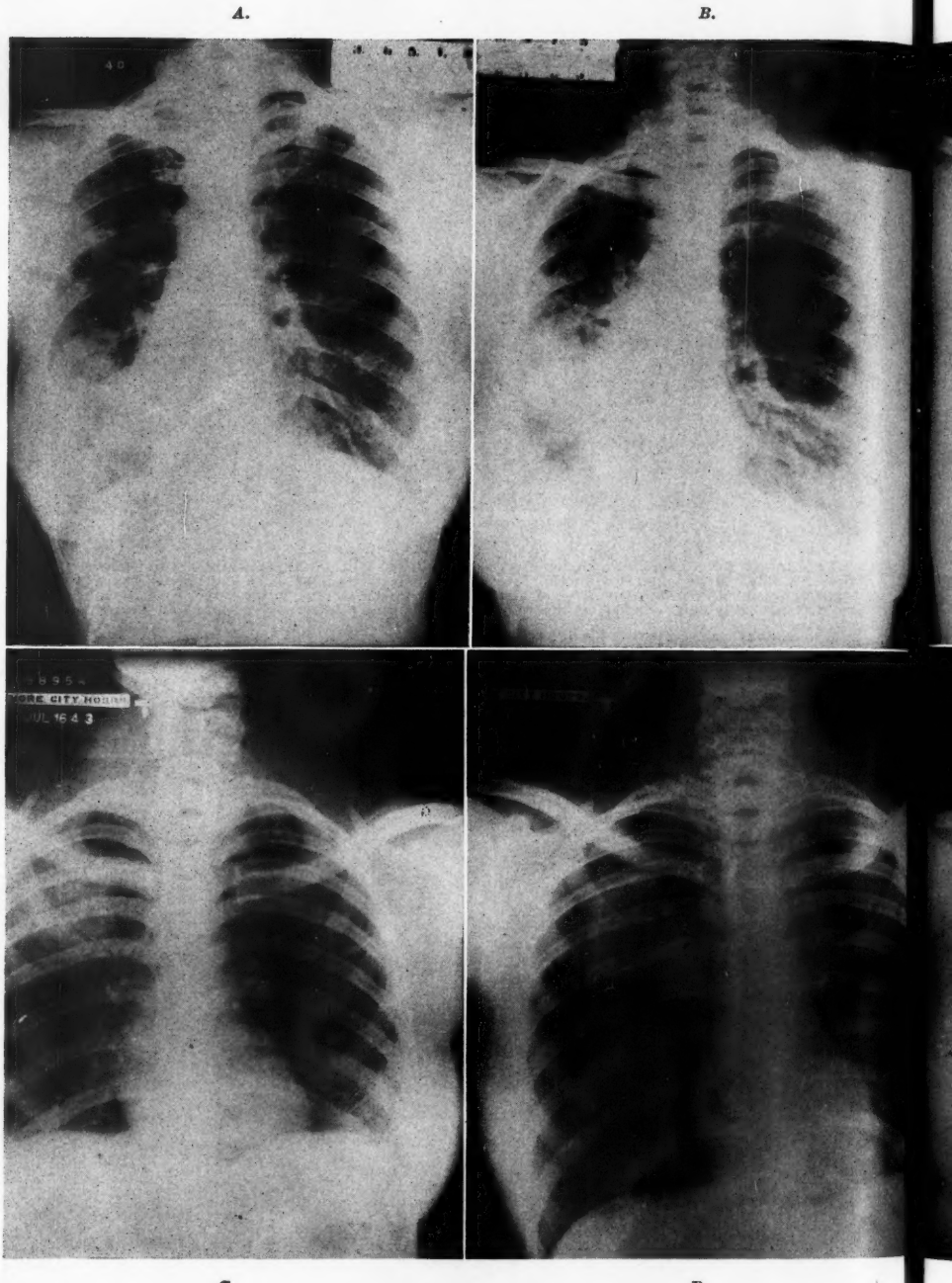
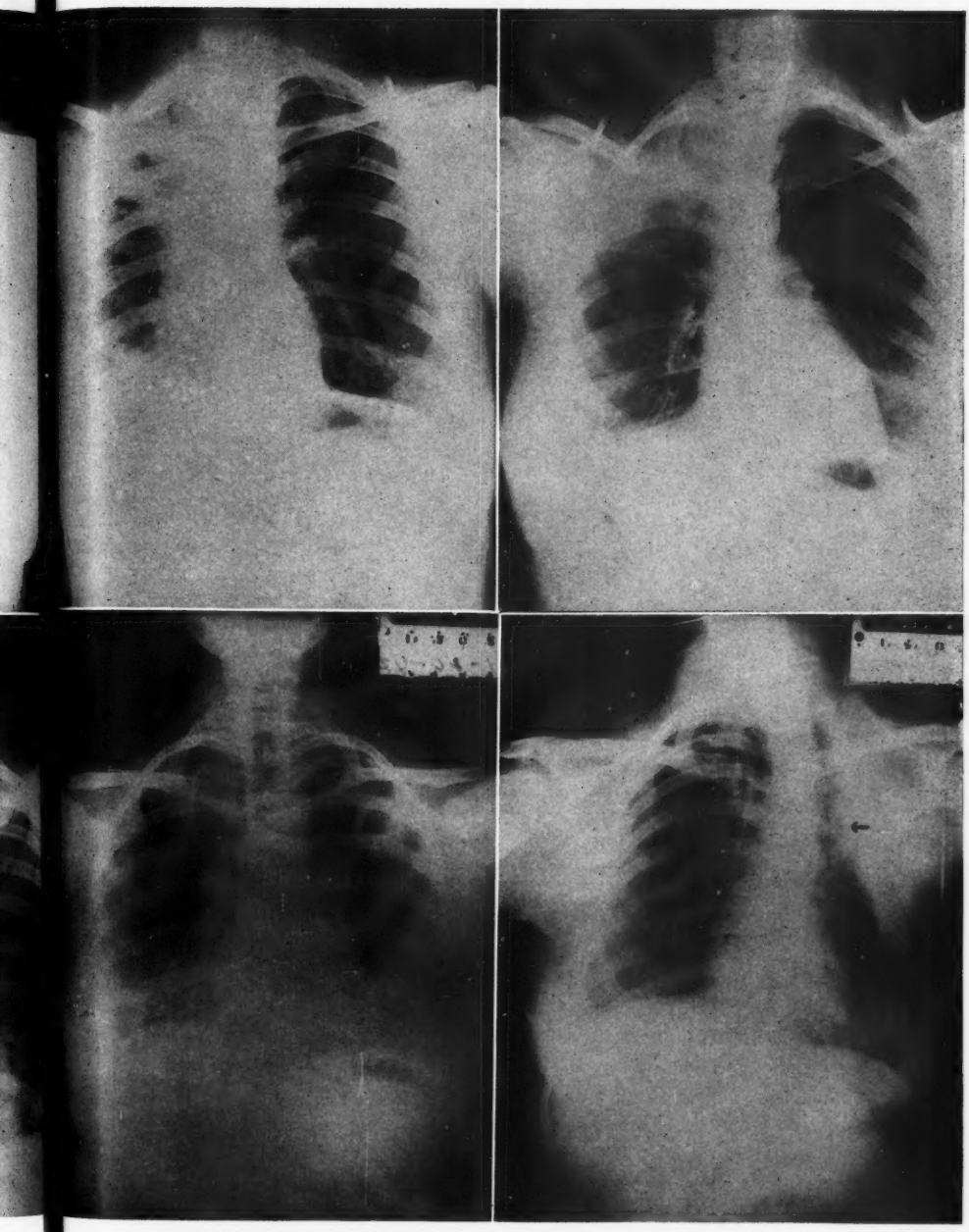


Fig. 5.—This series of roentgenograms forcibly demonstrates that collapse of pulmonary parenchyma per se is not the final criterion for closure of tuberculous cavities or healing of tuberculous pulmonary disease.

A, Before the phrenic nerve operation was done. *B*, Two years after permanent phrenic nerve paralysis. Note the excellent rise of the diaphragm; the diseased area has not collapsed or healed. *C*, Before pneumothorax was initiated. *D*, After pneumothorax was initiated. Pleural adhesions are present but they cannot account for the increase in the size of the cavity. The collapse of pulmonary tissue apparently has made the cavity larger.

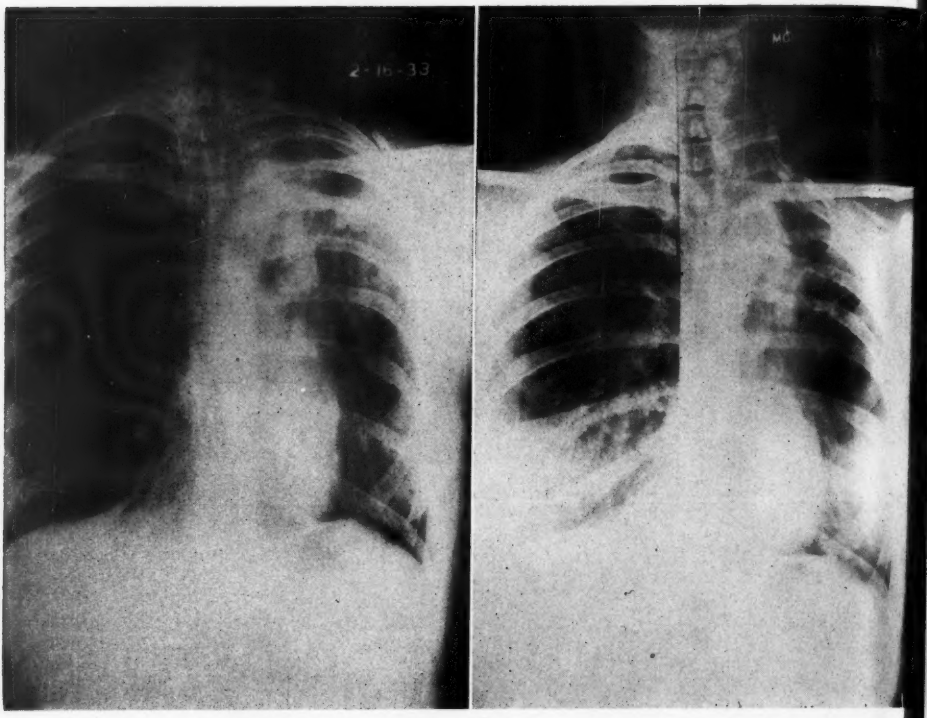


E. *F.*

G. *H.*

Fig. 5 (cont'd).—*E*, Before extrapleural pneumothorax was done. *F*, One year after extrapleural pneumothorax was established. The space became filled with fluid that was not infected. The cavity descended in the thorax and remained widely open. *G*, Before the standard thoracoplasty operation was done. *H*, One year after thoracoplasty. An excellent thoracoplasty has been accomplished as far as the bony thoracic cage is concerned but the cavity remained open.

2.0 per cent procaine for nerve block when the posterior ends of the ribs are to be resected. The operation is divided into easy stages so as to disturb the patient as little as possible (Figs. 7 and 8). An interval of at least one week is allowed between stages, but the interval may be lengthened to meet the needs of the patient.



A. *B.*

Fig. 6.—These photographs also reveal that pulmonary collapse per se is not the final criterion for healing of tuberculous pulmonary disease.

A, Before the thoracoplasty operation was done. *B*, Approximately five years after a poor partial Wilms-Sauerbruch thoracoplasty was performed. The collapse is minimal. The patient has remained well almost ten years.

The first stage is done in the neck, with the head rotated to the opposite side (Fig. 9). An incision is made from the posterior border of the sternomastoid muscle to the anterior border of the trapezius muscle about two finger-breadths above the clavicle. It is carried through the platysma muscle and cervical fascia. With medial retracton of the sternomastoid muscle and posterior retraction of the trapezius muscle the external jugular vein, supraclavicular nerves, spinal accessory nerve, phrenic nerve, the three scalene muscles, and the levator scapula muscle are exposed. The external jugular vein is divided and immediately deep to it is always a branch of the supraclavicular nerve. The branches of the supraclavicular nerve are then blocked with procaine. Care is taken not to injure the brachial plexus when the three scalene muscles are divided. Often the long thoracic nerve and always the dorsal scapular nerves are found in the substance of the scalene medius.[5] The posterior end of the first rib is then exposed and a section of at least one inch removed subperiosteally, beginning at the transverse process. The periosteum is then removed in order

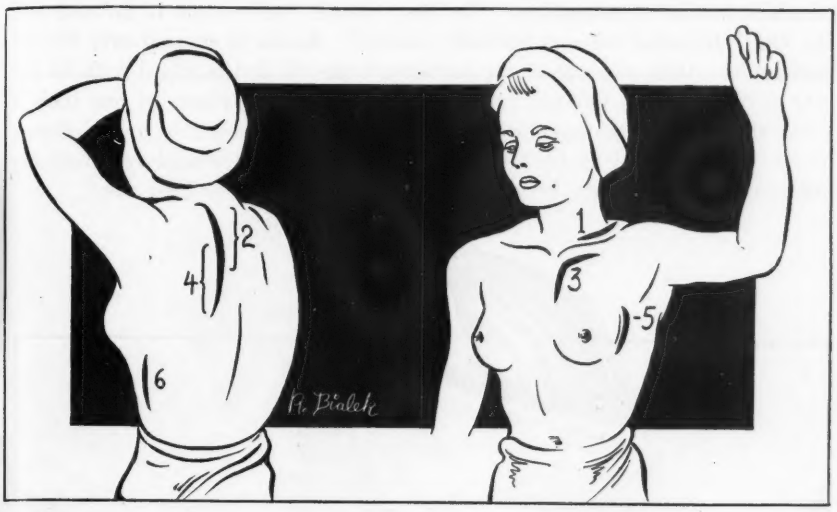


Fig. 7.—Drawings *A* and *B* illustrate the sites for the incisions in the relaxing thoracoplasty. The numbers indicate the order in which the operations are carried out.

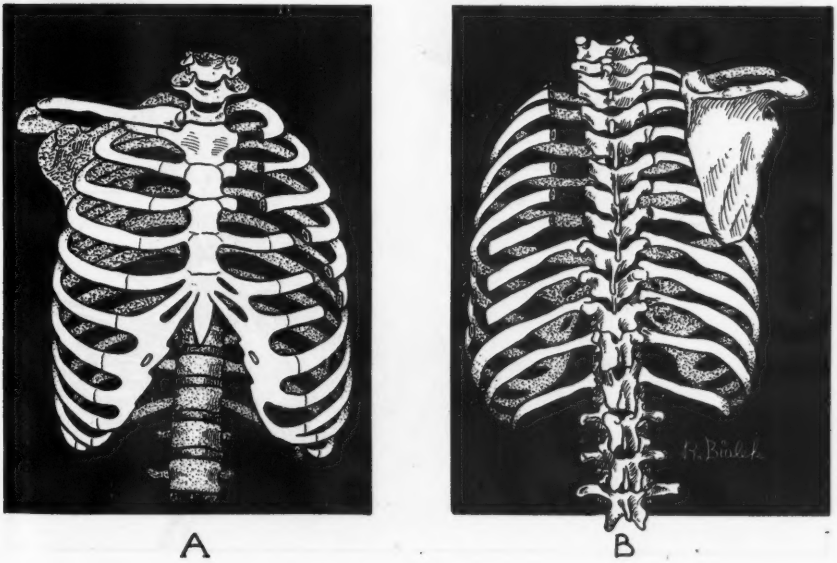


Fig. 8.—*A*, Drawing illustrates the third stage of the relaxing thoracoplasty where part of the first three costal cartilages and adjacent ribs have been resected, and also the fifth stage where a portion of the fourth, fifth, and sixth ribs have been removed.

B, A paravertebral resection of the first seven ribs and a portion of the transverse processes. This group comprises the ribs resected in the first, second, and forth stages. If the disease extends to the base, a paravertebral resection of the eighth, ninth, and tenth ribs with a portion of the transverse process is carried out. This is the seventh stage of the relaxing thoracoplasty. The seventh, eighth, and ninth ribs are shown resected in the posterior axillary line. This is the sixth stage of the relaxing thoracoplasty.

to prevent bone regeneration. The first thoracic nerve root is isolated and the first intercostal nerve is partially resected. Muscle is sutured over the cut bone ends. After removal of the periosteum the rib bed is wiped with 10 per cent formalin. The phrenic nerve is crushed over a distance of one inch if paralysis of the diaphragm is desired. It is usually desirable unless disease of the opposite lung contraindicates it. Closure of the wound requires only approximation of the deep cervical fascia, platysma muscle, and the skin.

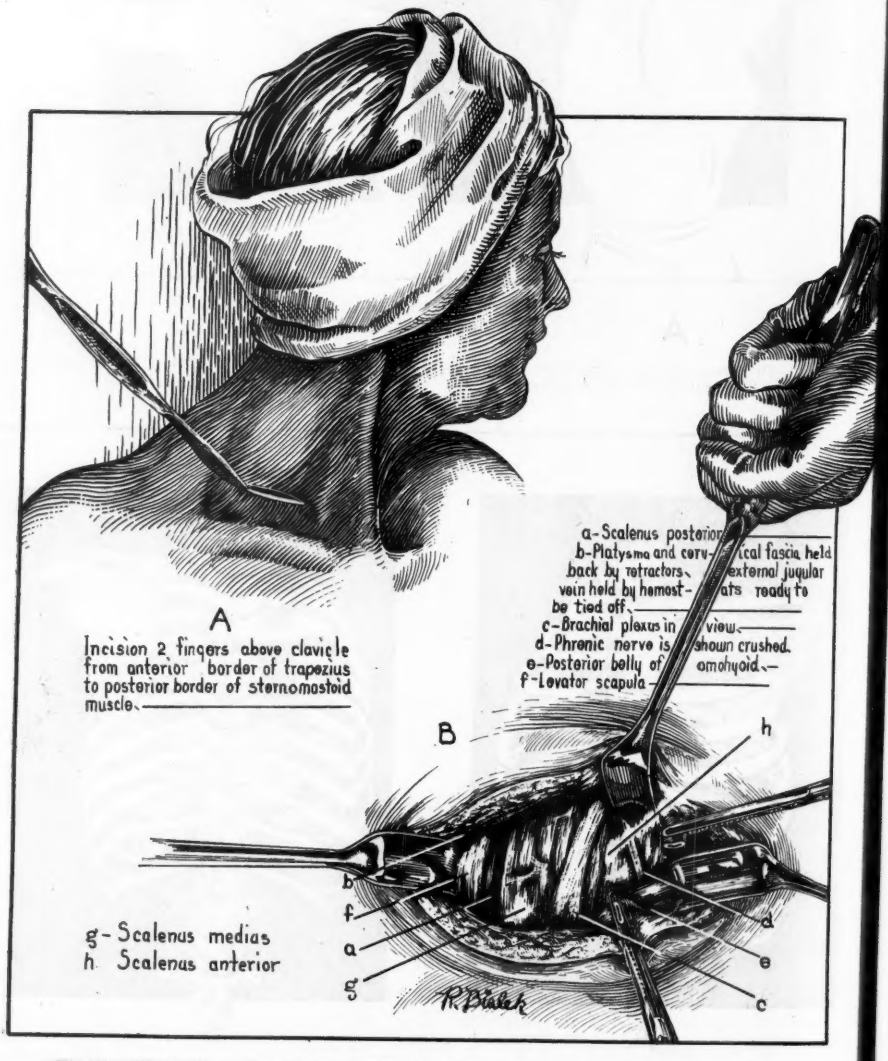


Fig. 9.—These drawings illustrate the first stage of the relaxing thoracoplasty operation. *A*, The site of the skin incision. *B*, The wound is shown opened. The scalene muscles and the brachial plexus are exposed.

The second stage is performed over the posterior ends of the upper ribs (Fig. 10). The patient is placed in a prone position, with the arm on the side of the operation reaching forward to make as much space as possible from the spinous processes of the vertebrae to the vertebral border of the scapula. An

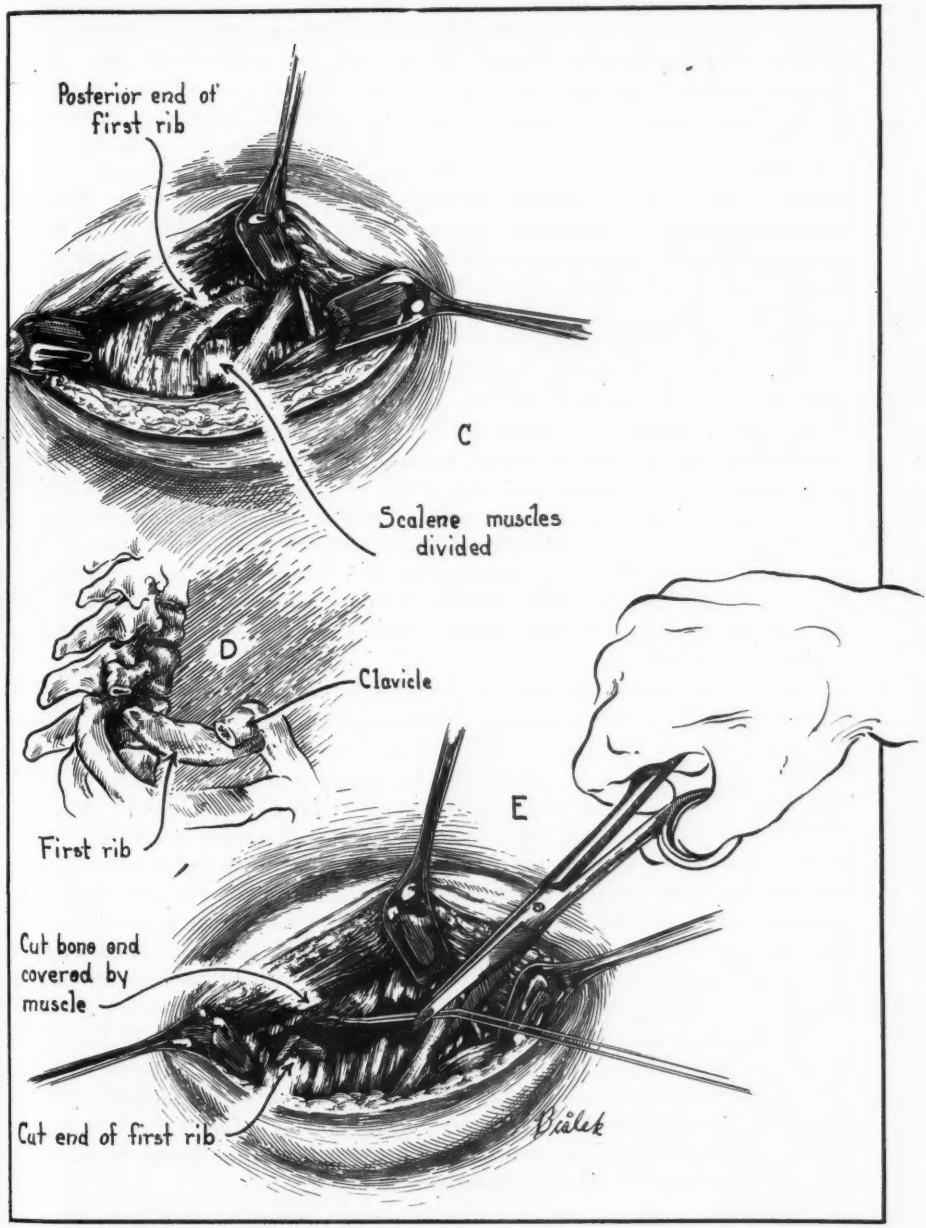


Fig. 9 (cont'd).—*C*, After the scalene muscles have been divided the posterior end of the first rib is revealed. *D*, An illustration of the section of the first rib that is removed. *E*, After a section of the first rib is removed the periosteum is excised. The rib bed is wiped with 10 per cent formalin. The cut bone ends are covered by muscle.

inverted hockey stick incision is made from the first rib to about the fifth, or about four to five inches long, and placed about three fingerbreadths from the midline. The trapezius, rhomboid minor, and a portion of the rhomboid major muscles are divided, thus exposing the erector spinae group of muscles, the serratus posterior superior muscle, and the posterior ends of the ribs. The serratus posterior superior muscle is divided. The erector spinae muscle is divided transversely and separated from the ribs and transverse processes. Two-inch sections of the second, third, and fourth ribs are removed subperiosteally with a part of their corresponding transverse processes. The intercostal nerves are isolated and divided. The periosteum is removed. Muscle is sutured over the cut bone ends. After removal of the periosteum the rib beds are painted with 10 per cent formalin. Care is taken to prevent bone regeneration between the rib ends and the transverse processes, and also to prevent bone regeneration between the ribs above and below. The wound is closed by approximating the divided muscles in layers and closing the skin.

The third stage of the operation is made with the patient in the supine position (Fig. 11). The incision is nearly right-angled, paralleling the medial third of the clavicle about one fingerbreadth below it, turning downward one fingerbreadth lateral to the sternal border, and ending at the fourth costal cartilage. The pectoralis major muscle is divided along this same line and retracted laterally. A two-inch section of costal cartilage and rib is removed from the first, second, and third ribs in a subperiosteally and subperichondrially manner. Usually the perichondrium and periosteum are then removed with ease. They can be so completely removed that painting with formalin may be omitted. The cut bone ends are covered with muscle and the wound is closed in layers with interrupted sutures.

The fourth stage is similar to the second (Fig. 10) and the fifth, sixth, and seventh ribs are resected in the identical manner used for the second, third, and fourth ribs. The corresponding intercostal nerves are not divided.

The fifth stage is performed with the patient in a supine or lateral position (Fig. 12). In women the breast is to be avoided by placing the incision lateral to it and retracting the breast medially. Since this is not necessary in men, the incision can be made directly over the ribs to be resected. One and one-half inch sections of the fourth, fifth, and sixth ribs are removed subperiosteally along the dominant line of Monaldi, that is, along a line from the first interspace at the sternum to the seventh interspace at the midaxillary line. The periosteum is removed. The rib bed is painted with 10 per cent formalin. The cut rib ends are covered over and the wound is closed in layers.

If the sixth stage is necessary it is done with the patient in the full lateral position. The incision is made directly over the ribs to be resected. One and one-half inch sections are removed subperiosteally from the seventh, eighth, and ninth ribs slightly anterior to the midaxillary line. The periosteum is removed. The rib beds are painted with 10 per cent formalin. Muscle is sutured over the cut rib ends and the wound closed in layers.

When the disease extends from the apex to the base of the lung, the seventh stage is needed and is done with the patient in the prone position. It is almost identical with the second stage of the operation except that the incision is made over the ribs to be resected. Sections are removed from the eighth, ninth, and tenth ribs and the operation is completed as in the second stage.

In reviewing the technical results of the operation it becomes strikingly evident that the regeneration of bone posteriorly is difficult to prevent. This

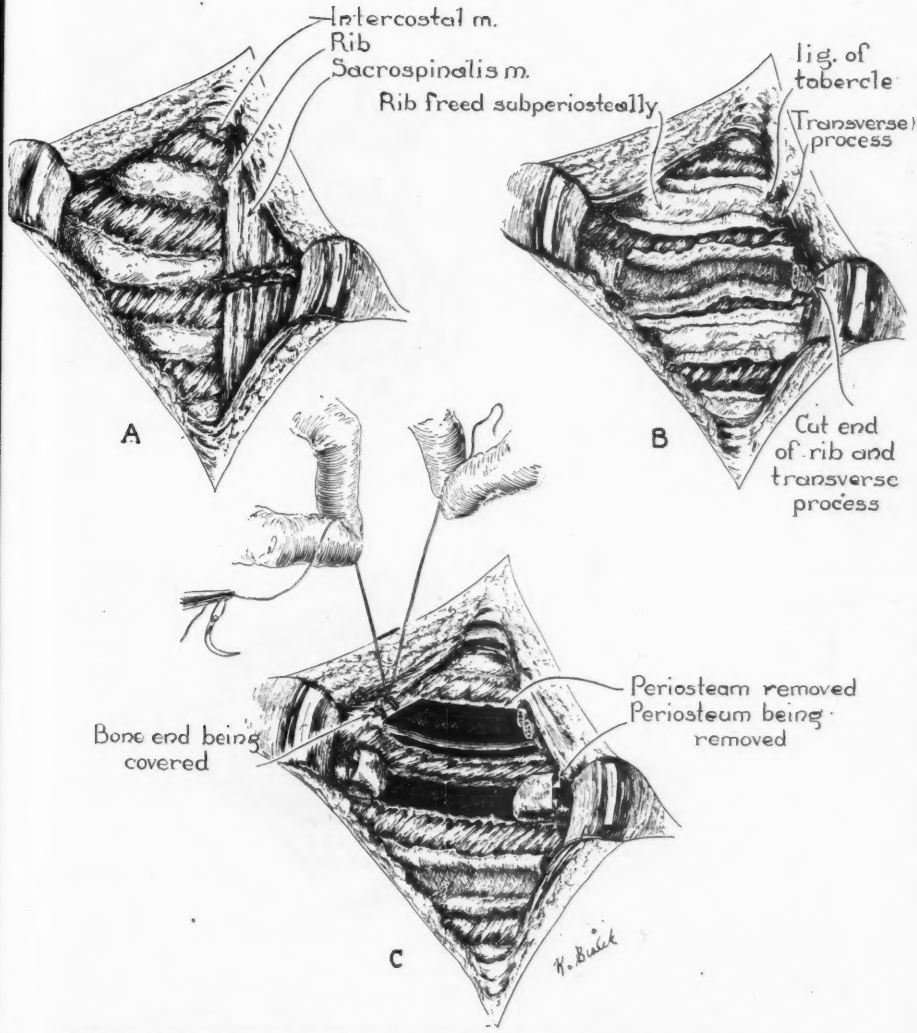


Fig. 10.—An illustration of the second stage of the relaxing thoracoplasty operation. *A*, The wound is shown after section and retraction of the trapezius, rhomboid minor, and major muscles. The sacrospinalis muscle (erector spinae) is shown divided and ready to be reflected above and medially and below and medially. *B*, The ribs are removed subperiosteally. A portion of the corresponding transverse processes are resected. *C*, The periosteum is resected. The cut bone ends are covered. The rib beds are painted with 10 per cent formalin.

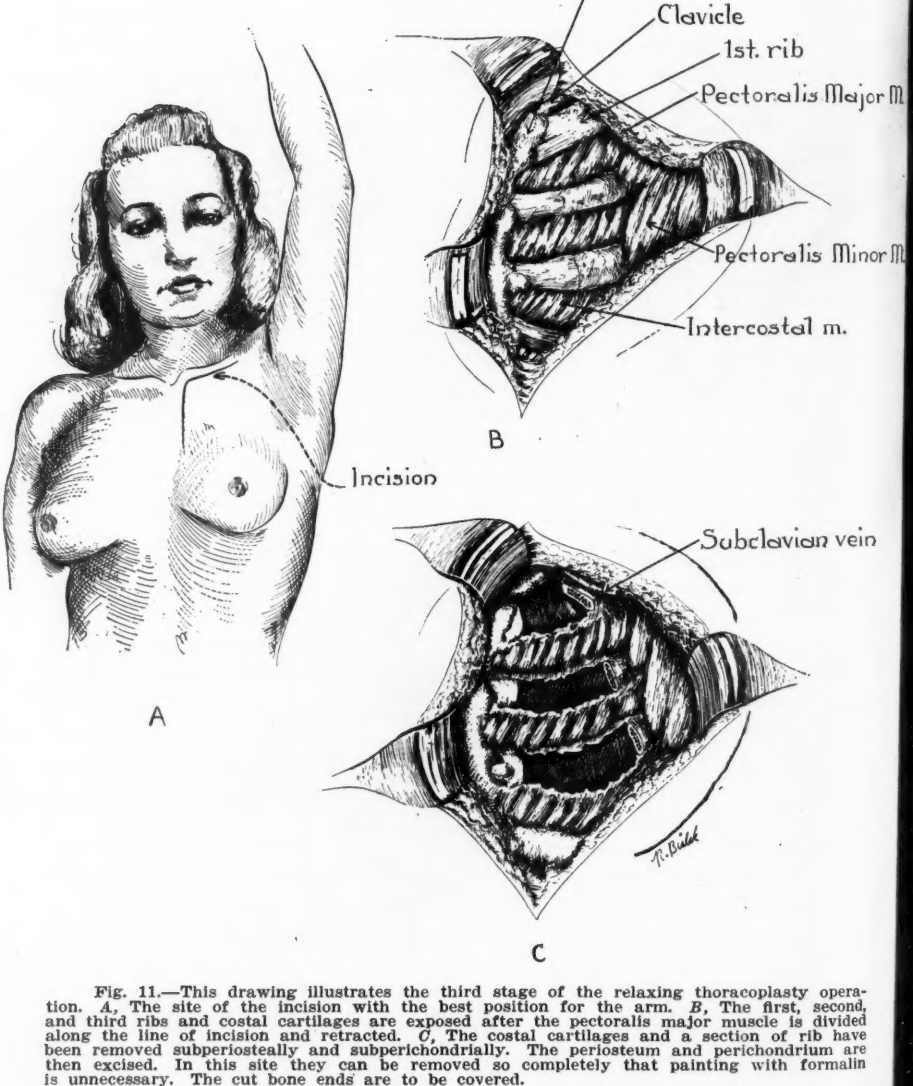


Fig. 11.—This drawing illustrates the third stage of the relaxing thoracoplasty operation. *A*, The site of the incision with the best position for the arm. *B*, The first, second, and third ribs and costal cartilages are exposed after the pectoralis major muscle is divided along the line of incision and retracted. *C*, The costal cartilages and a section of rib have been removed subperiosteally and subperichondrially. The periosteum and perichondrium are then excised. In this site they can be removed so completely that painting with formalin is unnecessary. The cut bone ends are to be covered.

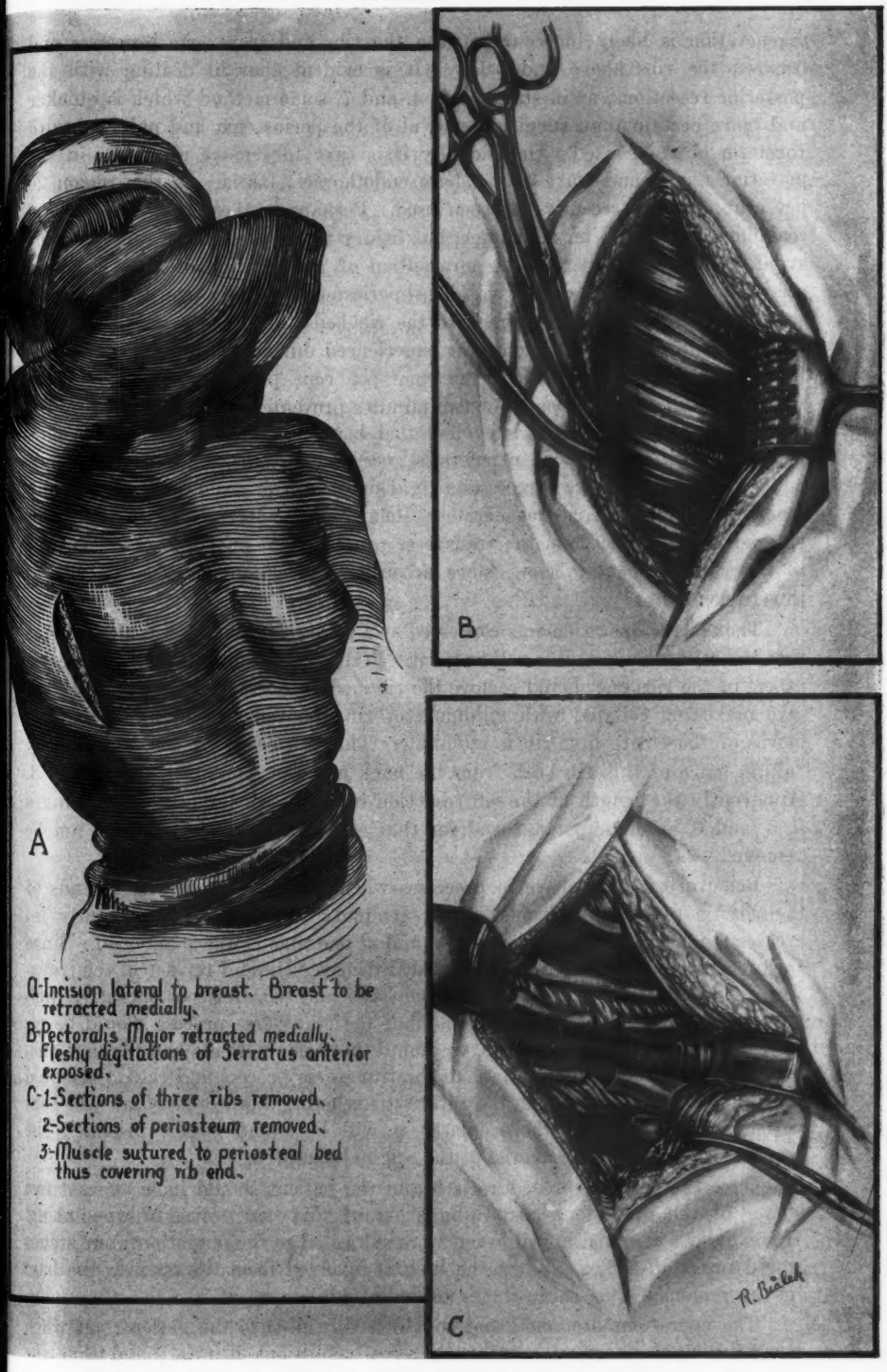

A
A-Incision lateral to breast. Breast to be retracted medially.
B-Pectoralis Major retracted medially. Fleshy digitations of Serratus anterior exposed.
C-1-Sections of three ribs removed.
2-Sections of periosteum removed.
3-Muscle sutured to periosteal bed thus covering rib end.
B
C

Fig. 12.—The fifth stage of the relaxing thoracoplasty operation. *A*, The site of incision in women is shown. In men it can be made obliquely and more medially, directly over the ribs to be resected. *B*, The digitations of the serratus anterior muscle are shown. *C*, Sections of three ribs have been removed subperiosteally. The periosteum is to be excised and the cut bone ends covered.

regeneration is likely to occur between the ribs and transverse processes and between the ribs above and below. It is evident that in dealing with the posterior resections, as in stages 1, 2, 4, and 7, some method which is quicker and more certain than surgical removal of the periosteum and painting with formalin must be used. Occasionally it is easy to remove all tissue in the posterior region and leave only a bare endothoracic fascia. In this region 20 per cent formalin recently has been used. Perhaps in these areas the electrocoagulation would be an advantage, but injury to the pleura and lung must be avoided. In other locations the prevention of regeneration of bone has been accomplished without difficulty. The periosteum usually can be removed easily. When formalin is applied to the rib beds the patients generally complain of pain even though none was experienced during the operation. It was found by Dr. Thomas O'Neill that one per cent procaine poured into the wound and allowed to remain for two minutes prevented the pain caused by the application of formalin. It is evident that bone regeneration defeats the purpose of relaxation. If bone regeneration occurs between the posterior cut ends of the ribs and transverse processes a rigid thoracic cage results. This is equally true if only one such rib regenerates. Relaxation is interfered with if the cut rib ends remain free from the transverse processes but anchor by bone growth to the ribs above and below, since accordion-like action between the ribs is thus prevented.

Though the operation was conceived as a pure relaxation it becomes evident that the collapse afforded is rather great. Perhaps in dealing with the posterior aspect of the ribs one should remove the rib medial to the angle, which will then give maximum collapse with minimum of rib removed. It might be that removal of the entire first rib is advisable. This can easily be accomplished by taking more of this rib both from the back and the front in stages 1 and 3. Apparently the length of the rib resection in front and laterally, as in stages 3, 5, and 6, is not important and for that reason long sections should not be removed.

Removal of the transverse processes when removing the posterior ends of the ribs is probably desirable. This seemingly simple procedure greatly increases the magnitude of the operation and at one time it was abandoned. Since the erector spinae muscle has been divided transversely and retracted, the transverse processes can be removed with more ease and with less postoperative difficulty to the patient. At least one-half of the transverse process should be removed. In reviewing the results, we found that some patients had perhaps one-half inch of rib remaining lateral to the transverse process and these presented uniformly poor results. If in the future the relaxing thoracoplasty must be converted into a standard thoracoplasty it will be found easier, provided the transverse processes are removed at the original operation.

Once the surgical procedure is begun the patient should have at least five stages of the operation. Anything short of this has proved disappointing. However, if a minimal apical lesion were subjected to the operation, four stages would probably suffice. When the lung is involved from the apex to the base by tuberculous lesions, seven stages are indicated.

The operations are small and should hardly disturb the patient, yet when operating upon those with rather hopeless conditions it was found that the original one-week interval between operations was not enough. Two weeks should be allowed to elapse between operations and if the patient is in poor

condition even more time can be allowed. Since the regeneration of bone will not occur, the interval is not important so long as the time allowed is not too short.

If this series of operations fails to bring about an arrest of the disease, the operation can be converted into a standard thoracoplasty. Patients who are not suitable candidates for the standard thoracoplasty might thus be brought safely to such a condition. Three of the patients reported here have been converted to a standard thoracoplasty, with one death. It is hoped, however, if the series of operations is technically correct this will not be necessary. The technical errors sometimes can be remedied by a localized revision of the relaxing thoracoplasty. Such a revision recently has been employed but not in this series of cases.

CLINICAL MATERIAL AND OPERATIVE RESULTS

The operative procedure was carried out on 33 patients. The total was made up of 15 white men, 6 Negro men, 9 white women, and 3 Negro women. Their ages varied from 19 to 55 years, with the greatest number occurring between the ages of 30 and 40 years. The first operation was done Dec. 19, 1941, and the first series of operations on one patient was completed Feb. 27, 1942. The last patient included in this series had the final operation completed April 9, 1943. Therefore, the longest period of observation was approximately two years and the shortest, ten months. Three patients had the relaxing thoracoplasty converted into a standard thoracoplasty and one of these died. Five deaths occurred in the series. Of the remaining 28 patients, the sputum examination revealed tubercle bacilli in 9 cases, 3 of these in Negro patients. Two of the patients with a positive sputum had the relaxing thoracoplasty converted into a standard thoracoplasty. In 19 patients the sputum examination on direct smear was negative for tubercle bacilli; of these only 2 had sputum cultures and both were negative (Table I).

TABLE I. END RESULTS

Total number of patients		33
Age		19 to 55 years
Period of observation after operation		10 to 24 months
Sputum negative		19
Sputum positive		9
Total deaths		5
Postoperative	2	
Amyloidosis	1	
Progression of disease	1	
Postconversion operation	1	

Conversion to a standard type of thoracoplasty was done in three of the patients who had a consistently positive sputum and roentgenographic evidence of open cavities approximately one year after the last relaxing operation. Only one operation was needed for conversion to a standard thoracoplasty. In each case the patient had been improved by the relaxing thoracoplasty. The two who are living have been too recently operated upon to predict adequately the final result. The patient who died had shown considerable improvement before the final operation. He died on the third postoperative day of an extensive flare-up of the disease in the contralateral lung. It is evident now that more time should have been given to stabilize the disease. Perhaps the surgical procedure at the conversion operation was too extensive.

Two of the five deaths followed the third and fourth relaxing operations, respectively. In both cases there was a hopeless amount of disease present

before the operations were undertaken. In each instance death came rather suddenly from an extensive flare-up of the disease in the contralateral lung. It is likely that more than one week should have been allowed between operations. The third death occurred about one year after the final relaxing operation and resulted from a continued progression of the bilateral pulmonary disease. The fourth death followed after the conversion thoracoplasty. The fifth death occurred in a patient who had been improved clinically. She developed tuberculous mastoiditis and underwent a mastoidectomy from which she recovered. She died of amyloid disease one year after the last stage of the relaxing thoracoplasty.

End results can be reported in several ways, and perhaps no classification is free of just criticism. Two methods of survey have been selected: first, whether the patient was a suitable candidate for a standard thoracoplasty; and second, whether a relaxing thoracoplasty, as planned, was actually accomplished. This is determined by roentgenographic studies of the bony thoracic cage irrespective of the lung fields.

Of the 33 patients, 12 were suitable candidates for a standard thoracoplasty. Ten of these now have a negative sputum, 2 have a positive sputum, none have had a conversion to standard thoracoplasty, and none died. There were 21 in the group not suitable for standard thoracoplasty; among these, 9 now have a negative sputum, 5 have a positive sputum, 3 have had conversion to standard thoracoplasty, and 4 died (Table II).

TABLE II. END RESULTS ACCORDING TO SUITABILITY OF PATIENT FOR STANDARD THORACOPLASTY

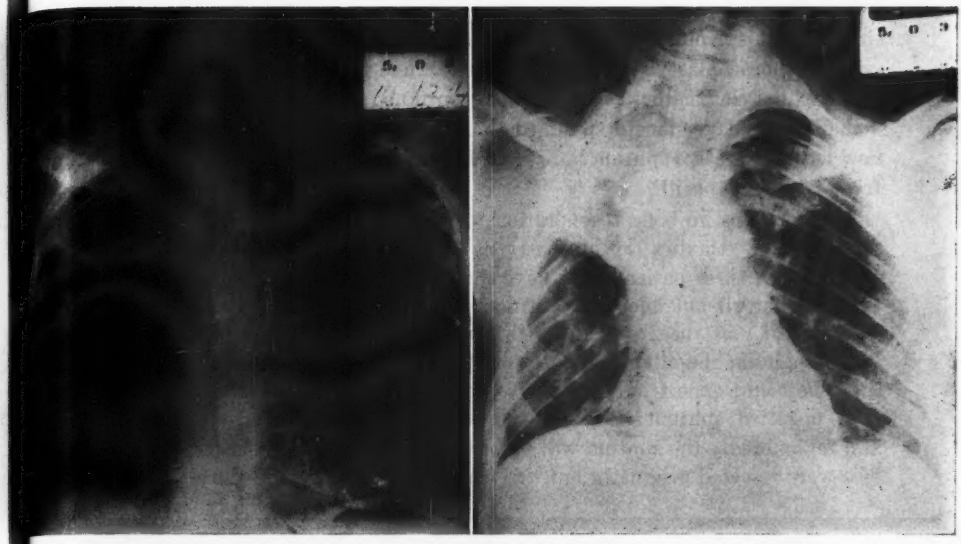
Patients suitable for standard thoracoplasty		12
Negative sputum	10	
Positive sputum	2	
Deaths	0	
Converted to standard thoracoplasty	0	
Patients not suitable for standard thoracoplasty		21
Negative sputum	9	
Positive sputum	5	
Deaths	4	
Conversion to standard thoracoplasty	3	

If the end results are to be judged according to the roentgenographic studies of the bony thoracic cage, there are 31 patients to be considered since there were only 2 operative deaths. These can be divided into three groups (Table III).

In 13 cases one or more ribs regenerated posteriorly and formed bone continuity with the transverse processes, thus nulifying the relaxing effect de-

TABLE III. END RESULTS ACCORDING TO ROENTGENOGRAPHIC STUDIES OF BONY THORACIC CAGE

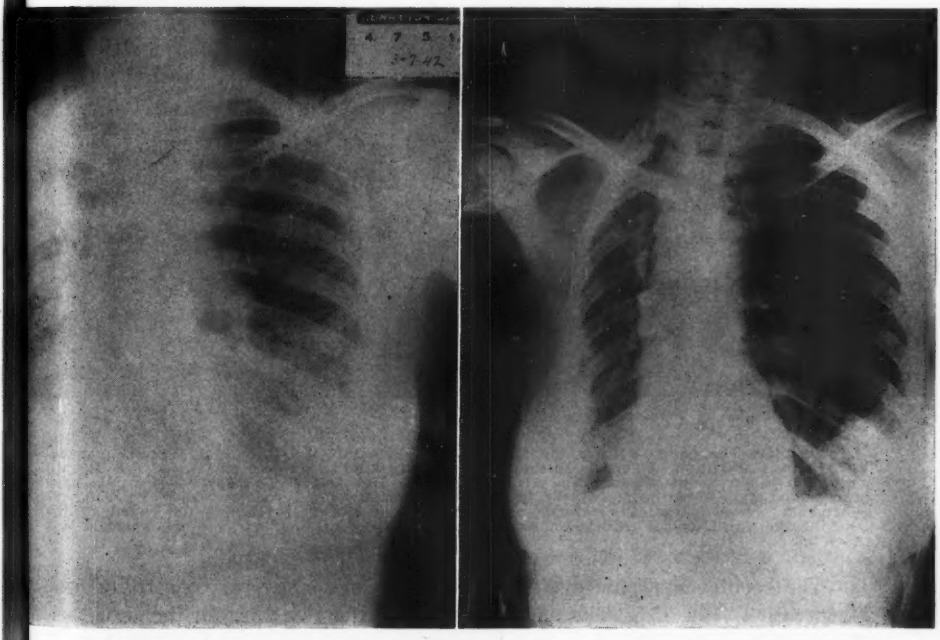
Good relaxing thoracoplasty (no bone regeneration)			12
Negative sputum	10		
Positive sputum	1		
Dead	1	(from amyloid disease)	
Poor relaxing thoracoplasty (definite bone regeneration)			13
Negative sputum	5		
Positive sputum	4		
Conversion to standard thoracoplasty	3		
Dead	1	(from continued progression of disease)	
Equivocal relaxing thoracoplasty			6
Negative sputum	3		
Positive sputum	3		



A. *B.*

Fig. 13.—The group classified as poor technical relaxing thoracoplasties is illustrated. Bone regeneration has occurred, thus resulting in a poor Wilms-Sauerbruch type of thoracoplasty.

A, Roentgenogram taken before operation. *B*, Roentgenogram about eight months later. The cavity is open. The sputum consistently contains tubercle bacilli. There has been definite bone regeneration rejoining the resected ribs to the transverse processes and in places to each other. Satisfactory end results cannot be expected in this group. The operation as outlined has not been accomplished.



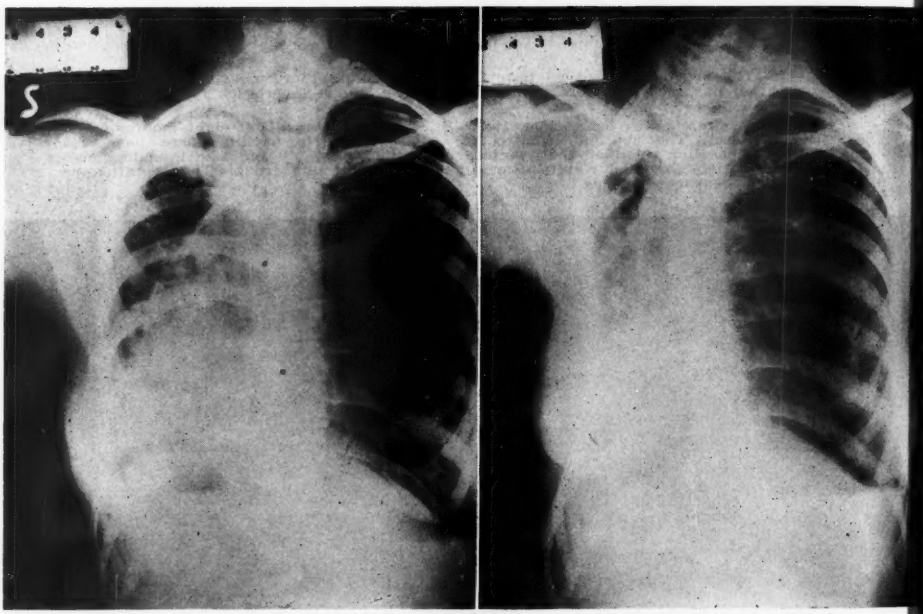
A. *B.*

Fig. 14.—Illustrations of the group classified as good technical relaxing thoracoplasties since roentgenographic studies of the bony thoracic cage reveal no regeneration of ribs.

A, Roentgenogram of the chest reveals a spherical cavity surrounded by a small zone of reaction. This appears to be a tension cavity. *B*, Fourteen months later, the same chest showing the results of a good technical relaxing thoracoplasty. The patient is clinically well and the sputum is consistently free of tubercle bacilli. There is no evidence of bone regeneration. A space is visible between the resected bone ends and the transverse processes. The ribs have not attached themselves to ribs above or below.

sired. In this group the operative procedure became a poor Wilms-Sauerbruch type[7] of thoracoplasty (Fig. 13). Eight of these patients now have sputum containing tubercle bacilli. One died from continued progression of the disease. In 3 there was conversion to standard thoracoplasty, with 1 death. Five patients now have a negative sputum but it is difficult to believe their sputum will remain free of tubercle bacilli.

In 12 cases no bone regeneration was revealed by roentgenographic studies and thus the relaxing thoracoplasty as originally intended was achieved (Fig. 14). Ten of these patients now have sputum free of tubercle bacilli and it seems evident that all but one will continue so. Their clinical appearance is that of good health. Of the 2 patients with sputum positive for tubercle bacilli, 1 died of amyloidosis; the other had such extensive pulmonary disease before operation that one could expect only a positive sputum at this time. One of the patients with negative sputum does not show resolution of the parenchymal disease and undoubtedly the sputum will become positive again. In this case not enough ribs were resected originally but this can be remedied by additional operation.



A. *B.*

Fig. 15.—The equivocal relaxing thoracoplasty group is illustrated. *A*, Roentgenogram taken before operation. There is a therapeutic pneumothorax on the right side. *B*, Roentgenogram taken about nine months after operation. The first three resected rib ends have been pulled tightly to the transverse processes and may well be anchored there by bone regeneration. Nevertheless, the resected posterior end of the first rib has descended to the level of the third dorsal transverse process, where it is anchored if bone regeneration has taken place.

The roentgenographic evidence in 6 cases was equivocal concerning bone regeneration (Fig. 15). The resected bone ends were together for the most part. This may have resulted from too little of the rib having been removed, from incomplete regeneration, or from the contracting power of the lung pulling the cut bone ends together. Three of these now have a sputum free of tubercle bacilli and in three the bacilli are present. One must view with suspicion the patients' ability to arrest their disease.

DISCUSSION

It is difficult to evaluate the results. Those patients who by roentgenographic studies of the ribs showed a satisfactory relaxing thoracoplasty had a correspondingly good lung parenchyma on the side operated upon. The clinical response, relief of symptoms, and gain in weight were uniformly good and the sputum was negative in a high percentage of cases. If the operation is based on sound principles these patients should not have an exacerbation of their symptoms because the thoracic cage is in a condition which will permit a continued arrest of the disease regardless of the number of years which elapse. Only time will bring the true answer.

The patients in whom a poor relaxing thoracoplasty was revealed by roentgenographic studies which showed regeneration of ribs have, for the most part, a continued presence of the parenchymal disease. It does not seem possible that they will improve. They are much like a poor result from a Wilms-Sauerbruch thoracoplasty. These patients can have the thoracic cage converted to a standard thoracoplasty or perhaps the rib cage can be revised to meet the requirements of a relaxing thoracoplasty. All the patients were clinically improved and many who were not suitable candidates for a standard thoracoplasty can now undergo such a procedure without too much risk.

The patients who have roentgenographically a type of thoracic cage which cannot be cataloged as either a good or a poor relaxing thoracoplasty give the most concern. Bone regeneration cannot be confirmed or denied. The cut bone ends posteriorly are tightly pulled together. It is impossible to determine whether the poor end result arises from a badly executed operative procedure or from the wrong selection of pulmonary disease for this type of operation. If this group results from the wrong type of disease being selected for the relaxing operation, it logically follows that the satisfactory results obtained when there is roentgenographic evidence of a good relaxing thoracoplasty may be caused by a favorable type of lung disease and not by the operation. Only those patients showing definite bone regeneration can be dismissed from further consideration on the ground that a relaxing thoracoplasty was not produced.

It appears that the patient with a giant cavity is not a suitable candidate for this operative procedure unless one is content with bringing the lesion and the patient to the condition where the relaxing thoracoplasty can be converted into a standard thoracoplasty. Apparently many patients who are not acceptable for a standard thoracoplasty can be brought to such a state by this procedure and thus it offers a form of treatment for the otherwise incurable case of pulmonary tuberculosis.

Whether this operative procedure will adequately arrest the disease in the tension type of lung has not been conclusively refuted or affirmed. Further study will be required to determine this point.

The patient with a concomitant disease or the one with some collapse of the contralateral lung is a good candidate for this operation. It also appears likely that the patient afflicted with the disease from the apex to the base on one side, but without giant cavities, is an ideal candidate for this operative procedure rather than for a complete standard type of thoracoplasty. The individual who has a pulmonary lesion which can be controlled by a one-stage standard thoracoplasty certainly should not be subjected to this type of operative procedure. In the future the individual whose disease can be controlled by a three-stage standard thoracoplasty may be treated by this type of thoracoplasty if the results remain encouraging.

It is likely that an extremely low operative mortality can be expected if the patients subjected to this operative procedure are in fair clinical condition. However, any operation carries its danger and here, as elsewhere, when the patient is in poor clinical condition fatalities will result.

CONCLUSIONS

1. Collapse of the lung in itself is not the complete answer to surgical treatment of pulmonary tuberculosis.

2. In pulmonary tuberculosis three general types of lungs with corresponding bronchi can be recognized: the lung with increased tension, the lung with neutral pressure, and the lung with decreased tension.

3. Based on the three general types of tuberculous lungs and upon the work of Monaldi, an operative procedure is outlined.

4. The results when viewed from certain perspectives are encouraging and certainly worthy of further study. Many patients who formerly had no hope of the disease being arrested are now brought within the realm of surgical treatment. Only time will determine the worth of the operative procedure, as well as its indications.

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THE IMPORTANCE OF ASCORBIC ACID (VITAMIN C) IN CHEST SURGERY

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THE study of the healing of wounds still presents a problem of great importance for the surgeon. If the scar is not strong enough after the operation to resist the forces which work against it, different complications may occur, according to the location and type of operation.

Concerning thoracic surgery, a bronchial fistula is an important and frequent complication after partial or total lung resection, resulting from a defective cicatrization of the bronchial stump. The satisfactory closure of the bronchus has been a constant problem for chest surgeons as may be well understood by the great number of articles and different techniques proposed in the medical literature. In the special case of the bronchus many different factors work against a good scar, such as the resistance of the bronchial cartilages and the constant variation of the pressure during respiration, cough, etc. Another complication in chest surgery of a defective scar is the disruption of the sutures of the gastro-esophageal anastomosis performed after an esophageal resection for cancer or cicatricial stenosis, resulting in a mediastinitis, empyema, and esophageal fistula.

Of course, two of the most important factors in the successful closure of the bronchial stump or gastro-esophageal suture are the pathologic state of the tissues involved and the surgical technique employed in the procedure. But, even with good technique and favorable local conditions, the development of the scar may be influenced by general factors, for instance, low blood protein level, allergic reactions against the suture material, and low blood ascorbic acid level.

Thompson, Ravdin, Rhoads, and Frank[45] have shown that the lowering of the plasma protein level may delay healing and even the most careful suture may give bad results. If the same animals are given a high protein diet the scars will be found normal. Kraissl, Kesten, and Cimiotti[27] found a very fast absorption of the catgut in animals previously sensitized with that material and they considered some patients may have the same allergic reaction against the sutures employed, resulting in a defective scar.

The importance of ascorbic acid in surgical cicatrization has been only recently recognized by experimental and clinical research, although since the seventeenth century navigators have known that wounds healed poorly after long voyages without fresh foods. In 1919 Aschoff and Koch[3] showed the pathologic alterations of the connective tissue in bones, muscles, and vessels of soldiers who died with scurvy. Wolbach[48, 49] and Wolbach and Howe[47] studied the alteration of the tissues during experimental scurvy in guinea pigs and showed that the proliferative power of the epidermis, endothelium, fibroblast, and osteoblast is normal, but there is a lack of the collagenous tissue. The

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number of fibroblasts in hematomas obtained surgically in animals with scurvy was the same as in normal animals, but there was no collagenous tissue surrounding and uniting these cells. The administration of ascorbic acid to these animals produced a normal scar, which was confirmed by V. Menkin, Wolbach, and M. Menkin.[30] Lanmans and Ingalls[28] and Taffel and Harvey[43] have studied the tensile strength of experimental wounds in animals with scurvy in which a lack of collagenous tissue was also proved histologically. These authors concluded that vitamin C plays an important role in the healing of experimental wounds in guinea pigs, and that there may exist in human beings a degree of vitamin deficiency that cannot be recognized by methods ordinarily used in physical examination. Bartlett, Jones, and Ryan showed in animals[6] and in human beings[7] that the tensile strength of the scar depends upon the amount of ascorbic acid in the tissues. Archer and Graham[1] observed the subscurvy state in patients with gastric and duodenal ulcer and Ingalls and Warren[23] showed low plasma ascorbic acid levels in surgical patients. Crandon, Lund, and Dill[11] studied extensively experimental scurvy in human beings during a long diet of six months without vitamin C and called attention to the determination of the amounts of ascorbic acid in the white cells and platelets. The importance of this determination was emphasized by Butler and Cushman.[10] They found that slight deficiency in ascorbic acid reserves did not affect the healing of a surgical wound, but when the signs of ascorbic acid deficiency are more evident the biopsy of a surgical incision showed that there was no healing of the wound, which was filled with unorganized blood clot. They observed the lack of intercellular substance and capillary formation, as had been found by Wolbach in the scorbutic guinea pig. Lund and Crandon[29] showed also low plasma ascorbic acid levels in some patients with disruption of the incisions after laparotomies, considering this factor as an important one in the etiology of the defective scar in that complication. I tried also[53] to study the resistance and the histology of scars obtained in normal and scorbutic guinea pigs, which are incapable of accomplishing the synthesis of ascorbic acid, when they are deprived of natural sources. One group of animals was submitted to a regime which made them free of ascorbic acid in the blood, as observed in extractions by cardiac puncture. These animals, as well as normal controls, underwent a laparotomy and the operative scar was artificially broken by elevation of the intra-abdominal pressure at the fourth, sixth, eighth, tenth, twelfth, and fifteenth days of the postoperative period. It was ascertained that to rupture the scars of normal animals a pressure was required five times higher than that required to rupture identical scars of animals under experimental scurvy (Fig. 1).

A second group of animals was submitted to a laparotomy and a gastrostomy using the same technique in normal and scorbutic animals. These animals were sacrificed by anesthetic syncope in different days of the postoperative period and their scars were studied histologically by the Mallory specific stain. It was ascertained that the number of fibroblasts that grew in the scars was practically the same in the two groups of animals; however, in the animals under relative scurvy the quantity of intercellular collagenous tissue varied with the intensity of the scurvy, being almost absent among the animals with complete scurvy.

It has been proved by many authors that the blood ascorbic acid level is lower than the normal in many surgical and clinical conditions. Bartlett, Jones, and Ryan[5] found in patients with such different diseases as tuberculosis, ulcerative colitis, osteomyelitis, and gastric cancer, that the average level in the

plasma was 0.43 mg. per 100 c.c. (normal considered between 0.8 to 1.2) and that after the operation the level in the blood was found still lower and the amount of ascorbic acid increased in the urine. Ingalls and Warren[23] studied twenty patients with peptic ulcer and found the average of 0.29 mg. per cent of plasma ascorbic acid. Archer and Graham[1] called attention to the very low levels in patients with gastric and duodenal ulcer during medical treatment by diet. Minnich, Wright, Moore, and Spies[34] showed that the whole blood and plasma ascorbic acid determinations made on seventy patients in the nutrition clinic of the Hillman Hospital indicated that fifty-five of these persons had a concentration lower than that in normal controls.

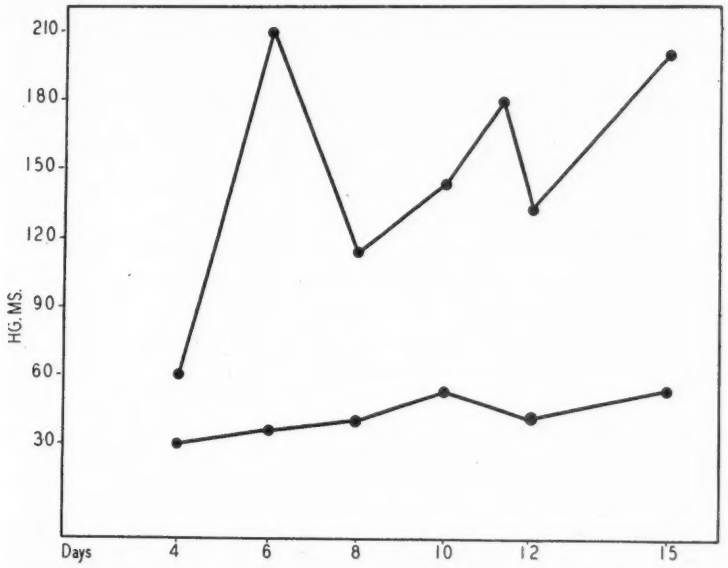

Fig. 1.—Pressures required to rupture experimental wound scars with and without vitamin C. Upper curve shows the higher pressures required in the normal control guinea pigs. The lower one gives the results in the animals without Vitamin C in the blood. The pressures are expressed in millimeters of mercury.

VITAMIN C IN THORACIC SURGICAL PATIENTS

The amount of vitamin C in both the blood and the tissues of patients with chronic surgical diseases of the lung and esophagus was determined. Twenty-two patients were studied before and after operation. The average found just after the admission of the patients was 0.15 mg. per cent of plasma ascorbic acid. Among these patients only one had a normal blood level and nine showed complete absence of ascorbic acid in the plasma.* The total and fractional proteins were tested in all patients continuously to avoid a mistake in the interpretation of the results.

Besides that, the operation by itself reduces considerably the plasma ascorbic acid level, according to the danger of the surgical procedure and the complications in the postoperative period. If we study the findings obtained from the plasma of the only patient observed to have normal ascorbic acid before operation we can see that this level was very low during the time that the cicatrization was in progress.

*The method used for the determination of ascorbic acid was that devised by Mindlin and Butler.[22]

CASE REPORTS

CASE 1.—W. W., a 29-year-old white man, entered Barnes Hospital, Nov. 13, 1944, with a history of hemoptysis for a period of fifteen years, which had been very severe in the three years before admission. This patient was studied in another hospital and he was referred to us for a right middle lobe lobectomy after an unsuccessful attempt was made to stop the bleeding by right pneumothorax.

Physical examination showed clubbing of the fingers and expiratory râles just to the right of the sternum in the fourth intercostal space. At the bronchoscopic examination the middle lobe orifice showed a definite amount of swelling, and some increase of bloody secretion was seen coming from the middle lobe bronchus. No evidence of tumor was found and biopsy of the bronchial mucosa was negative.

The ascorbic acid level in the plasma was tested on the first and third preoperative days and was found to be normal (1.2 mg.) (Fig. 2); the total and fractional proteins were also found normal (total proteins 6.3 Gm. per cent, albumin 4.2 Gm. per cent and globulin 2.1 Gm. per cent).

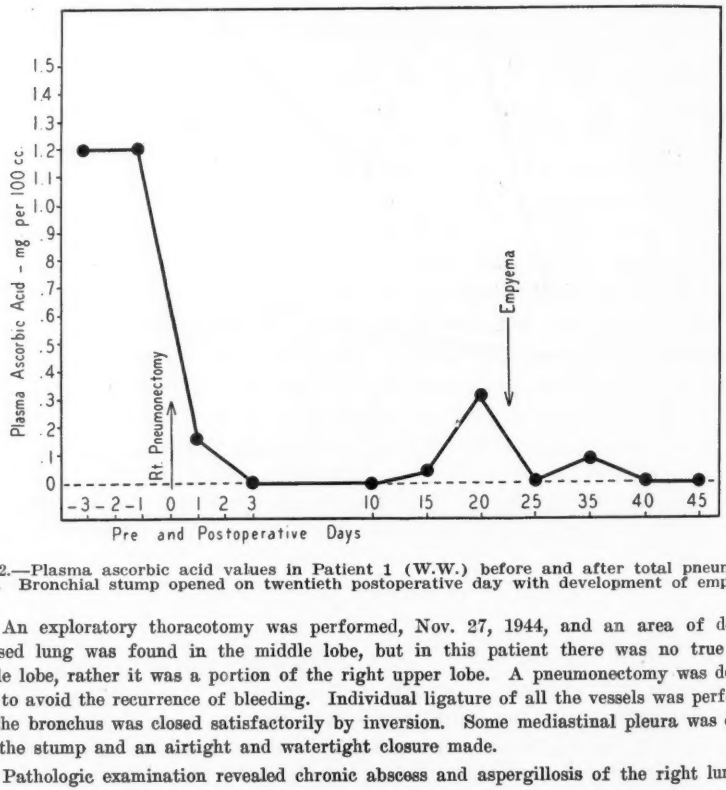

Fig. 2.—Plasma ascorbic acid values in Patient 1 (W.W.) before and after total pneumonectomy. Bronchial stump opened on twentieth postoperative day with development of empyema.

An exploratory thoracotomy was performed, Nov. 27, 1944, and an area of definite diseased lung was found in the middle lobe, but in this patient there was no true right middle lobe, rather it was a portion of the right upper lobe. A pneumonectomy was decided upon to avoid the recurrence of bleeding. Individual ligature of all the vessels was performed and the bronchus was closed satisfactorily by inversion. Some mediastinal pleura was drawn over the stump and an airtight and watertight closure made.

Pathologic examination revealed chronic abscess and aspergillosis of the right lung.

The amount of plasma ascorbic acid and proteins revealed the facts shown in Table I.

On the twentieth postoperative day, when the administration of penicillin was discontinued, the patient developed an empyema and he expectorated some gentian violet which had been introduced in the pleural cavity. Thoracotomy tube with closed drainage was instituted and some days after that an open drainage. The patient was discharged from the hospital with the fistula (Fig. 2).

Comment.—The observation of this patient shows that even though he had a normal plasma ascorbic acid level before the operation, postoperatively this level reached almost zero and remained very low for many days. The level gradually rose until the occurrence of an empyema, when it again fell and

TABLE I

DAY	ASCORBIC ACID (MG. %)	TOTAL PROTEINS (GM. %)	ALBUMIN (GM. %)
Third preoperative	1.2	6.3	4.2
First preoperative	1.2	6.2	4.2
First postoperative	.16	5.0	3.2
Third postoperative	0		
Tenth postoperative	0	6.5	4.2
Fifteenth postoperative	.04	6.0	3.4
Twentieth postoperative	.3		
Twenty-fifth postoperative	0		
Thirty-fifth postoperative	.10		
Fortieth postoperative	0		
Forty-fifth postoperative	0	6.5	3.9

remained low during the time in which the process of cicatrization of the bronchus was in evolution. This occurred despite the fact that he was encouraged to eat a general diet.

In other cases, therefore, an attempt was made to raise the plasma ascorbic acid level before and after operation, so as to aid in the scar formation. In order to do this the patients were given 1,000 mg. of ascorbic acid in a single period of twenty-four hours. This was divided into small doses of 100 mg. at a time. In a typical case, testing the plasma levels before and after the operation, it was seen that in twenty-four days of postoperative observation the level in the plasma was progressively increased to 0.85 mg. per cent, which is almost the normal level. The increase of ascorbic acid in the plasma was slow, although large doses were employed. It was observed also that the ascorbic acid level in the white cells and platelets was 40 mg. per cent and 42 mg. per cent, respectively, nineteen and twenty-four days after the operation.

CASE 2.—B. E. E., 18 years old, white, female, was admitted to Barnes Hospital with a history of bronchiectasis since childhood and the bronchograms showed dilated right lower lobe bronchi. She also had evidence of bilateral sinusitis and nasal polyps. A bilateral Caldwell-Luc operation and removal of nasal polyps were performed in November, 1944. The patient returned to the hospital Dec. 15, 1944, for treatment of the bronchiectasis and two days before the operation it was ascertained that she had no ascorbic acid in the plasma. Ascorbic acid, 1,000 mg., was prescribed each day and we verified that the level in the plasma was improved very slowly. After 3.0 Gm. of ascorbic acid the plasma level was still practically 0.0 milligram per cent. In the postoperative period, it was possible to increase progressively the amount in the plasma to 0.30, 0.52, 0.72, 0.80, and 0.85 mg. per cent (Fig. 3).

This patient had a very difficult right lower lobe lobectomy and during that difficult operation numerous dense adhesions were noted around the right lower lobe which required considerable sharp and blunt dissection. It was impossible to do an individual ligation of the vessels and bronchus, therefore, a mass ligation by means of a tourniquet was performed. The pleural cavity was drained with two No. 30 F. catheters, one in the posterior and another in the anterior axillary line. The next day after the operation she showed signs of bronchopleural fistula which was proved by the amount of air which escaped through the empyema bottle. An empyema developed which required posterior open drainage. The patient was discharged, Jan. 23, 1945, in good condition but still with drainage of the right pleural cavity.

Comment.—This observation showed that although the operation had been difficult and grave complications had occurred in the postoperative period, it was possible to maintain the plasma ascorbic level in an almost normal condition. The bronchial fistula which occurred the first postoperative day was undoubtedly due to the technique employed during the operation. The tourniquet mass ligation is recognized as a poor technique which should be employed only when an individual ligation is impossible.

A single determination of the ascorbic acid of the plasma is not the best index of the Vitamin C condition of the patient, because there are changes in the plasma ascorbic acid level according to the addition or withdrawal of ascorbic acid from the diet. Wright, Lilienfeld, and McLenathan[51] proposed the determination of the vitamin C saturation of the body, testing the plasma levels during five hours after an intravenous dose of 1 Gm. of ascorbic acid. This test gives a better estimation of the actual state of vitamin C saturation of the tissues. Because of the possibilities of variations in the excretion of the ascorbic acid due to an impaired renal function, the vitamin C urinary output should be tested at the same time. The saturation curve of a patient who came to the hospital with zero ascorbic acid in the plasma was studied. One gram of vitamin C was given to him and the blood was tested each hour; it was found that in four and one-half hours the level in the plasma came to zero again, which signified a great deficiency. This patient was given 1 Gm. of ascorbic acid every day and the level in the plasma increased to 0.50 mg. per cent. Then, another

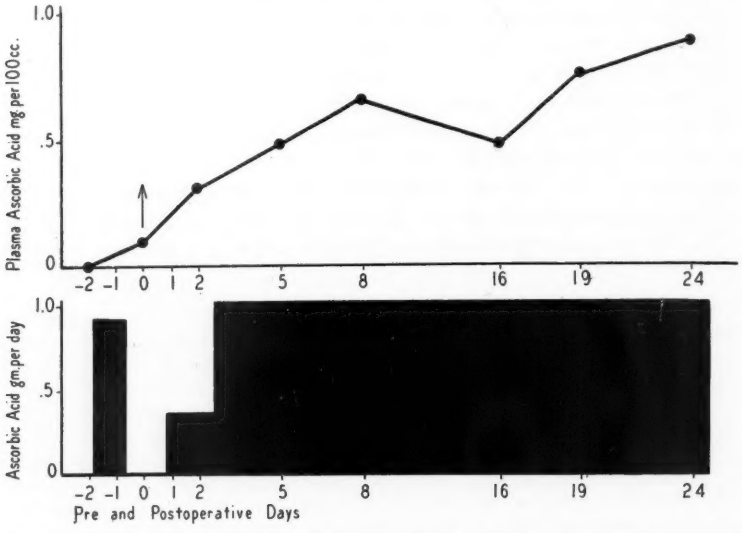

Fig. 3 (Case 2).—Patient had lobectomy for bronchiectasis. On admission no ascorbic acid was present. Administration of 1,000 mg. daily finally brought up level to normal but bronchial stump opened up promptly after operation while plasma level was still very low.

saturation curve showed that after the administration of 1 Gm. of ascorbic acid, the level in the plasma came down slowly and yet stayed higher than before the administration of the drug. When the patient is completely deprived of ascorbic acid, or its concentration in the tissues is low, the ascorbic acid which is not eliminated by the kidneys is absorbed by the tissues and the level in the plasma therefore falls quickly. When the tissue concentration is higher the level of the plasma will fall more slowly (Fig. 4).

CASE 3.—R. P., a 46-year-old white man, entered Barnes Hospital, Dec. 26, 1944, with history of cough, blood-tinged sputum, anorexia, and weight loss of ten pounds during the last six months. He also complained of sharp pain in the left side of the chest during the previous month.

The physical examination revealed the trachea to the left, louder breath sounds at the left base, and a short harsh apical systolic murmur of the heart. The bronchogram revealed an occlusion of the left lower lobe bronchus and a biopsy specimen obtained during the bronchoscopy confirmed the diagnosis of bronchiogenic carcinoma, therefore, a pneumonectomy

was decided upon. Three days before the operation the plasma ascorbic acid was found to be zero and a saturation test was done (Fig. 4). An exploratory thoracotomy was performed Jan. 25, 1945, and an inoperable bronchiogenic carcinoma of the left lung was found. Three days after the operation the patient was given 1 Gm. of ascorbic acid daily; the plasma ascorbic acid level was tested frequently and after a total of 9.0 Gm. were given it remained 0.50 mg. per cent. Another saturation test was performed nineteen days after the operation before the discharge of the patient when we observed a different curve. The plasma ascorbic acid level came down slowly and stayed at 0.80 mg. per cent.

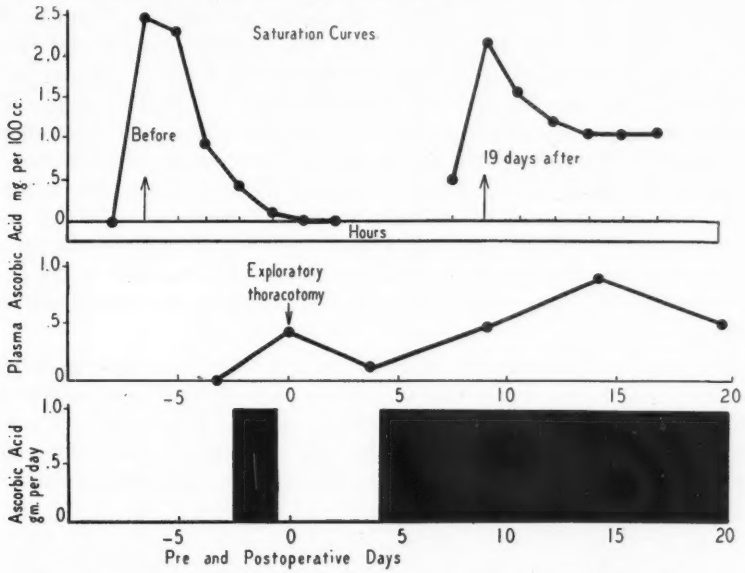

Fig. 4 (Case 3).—Saturation curves in a patient who entered with no ascorbic acid in the plasma. See text.

Comment.—The observation of this patient shows that 1 Gm. of ascorbic acid daily may not be enough to correct promptly the ascorbic acid level in the plasma. It is also seen that the saturation test gives an idea about the amount of ascorbic acid in the tissues. The saturation curves obtained before and after the administration of vitamin C are different.

Besides the saturation curve a good idea about the amount of ascorbic acid in the body or the degree of saturation or depletion of the tissues may be obtained by measuring the ascorbic acid content of the blood cells. The determination of the ascorbic acid in the blood cells was practically employed only after the work of Butler and Cushman.[10] These authors found in normal subjects the following averages: plasma, from 0.8 to 2.5 mg. per cent; red cells, from 0.4 to 1.5 mg. per cent; white cells and platelets, from 25 to 38 mg. per cent; whole blood, from 0.8 to 1.9 mg. per cent. The importance of the determination of the ascorbic acid content of the white cells and platelets was also emphasized by Crandon, Lund, and Dill.[11] One of these authors deprived himself of ascorbic acid for a period of six months and during this time a surgical incision was made and studied histologically. The cited authors showed that the plasma level dropped irregularly to zero in forty-one days and that the ascorbic acid level in the white cells dropped to 4 mg. per cent on the eighty-second day, later reaching zero. After three months of complete absence of ascorbic acid in the food, and when the plasma ascorbic acid had been zero for forty-four days, a wound was made in the right mid-back of the subject. Ten days later

a biopsy of this wound showed good healing, as compared with a normal control. At the end of 182 days, after the plasma ascorbic acid had been at zero for 141 days, the white cell platelet ascorbic acid at zero for sixty-one days, and petechiae apparent over the lower limbs for twenty-one days, a similar wound was made in the left mid-back. A biopsy was made on the tenth postoperative day and beneath the skin, which appeared well healed, there was no healing of the wound, which was filled with an unorganized blood clot. Sections showed lack of intercellular substance and capillary formation, as had been found by Wolbach in wounds of scorbutic guinea pigs. The subject received 1.0 Gm. of ascorbic acid intravenously and after ten days another biopsy showed perfect cicatrization. The ascorbic acid was administered by a saturation regime which consisted of daily intravenous injections of 1.0 Gm. of ascorbic acid following which hourly plasma and urine determinations were made. On the first day the plasma C content fell very rapidly during the first three hours after the injection, reaching zero at the end of five hours. After each day the initial plasma and also the white cell platelet levels were higher than on the previous day and after the injection of 1.0 Gm. of ascorbic acid, the level in the plasma came down slowly and yet remained higher than before the administration of the drug.

The plasma and white cell levels before and after some pneumonectomies were tested and it was found that the plasma ascorbic acid came to zero after the operation but the white cell platelet level did not change. In such patients there is a deficiency of ascorbic acid, but this deficiency is not dangerous because the blood still contains an adequate amount of ascorbic acid for the tissues.

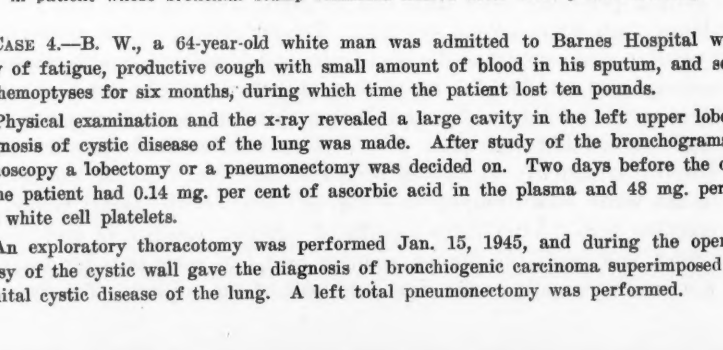

Fig. 5 (Case 4).—Curves showing ascorbic acid levels in white cells and plasma respectively in patient whose bronchial stump remained healed after total pneumonectomy.

CASE 4.—B. W., a 64-year-old white man was admitted to Barnes Hospital with a history of fatigue, productive cough with small amount of blood in his sputum, and several small hemoptyses for six months, during which time the patient lost ten pounds.

Physical examination and the x-ray revealed a large cavity in the left upper lobe and a diagnosis of cystic disease of the lung was made. After study of the bronchograms and bronchoscopy a lobectomy or a pneumonectomy was decided on. Two days before the operation the patient had 0.14 mg. per cent of ascorbic acid in the plasma and 48 mg. per cent in the white cell platelets.

An exploratory thoracotomy was performed Jan. 15, 1945, and during the operation a biopsy of the cystic wall gave the diagnosis of bronchiogenic carcinoma superimposed on a congenital cystic disease of the lung. A left total pneumonectomy was performed.

The ascorbic acid was tested at the third, seventh, and twelfth postoperative days and we determined that the level in the plasma came to zero three days after the operation but the level in the white cells remained unchanged. The patient was discharged eighteen days after the operation in good condition. The bronchial stump remained solidly healed. (Fig. 5.)

Comment.—When no ascorbic acid is found in either the plasma or the white cell platelets a dangerous deficiency of vitamin C is present. In a state like that an operation is extremely dangerous because no sutured areas will heal securely. There was only one patient in such a condition.

CASE 5.—E. F., a 61-year-old white man, was admitted to Barnes Hospital, Oct. 14, 1944, with a history of progressive dysphagia for four months and nineteen pounds of weight loss. After an x-ray examination of the esophagus, esophagoscopy, and biopsy of an esophageal tumor, the diagnosis of epidermoid carcinoma 25 cm. below the incisors was made. Oct. 19, 1944, a Janeway gastrostomy was performed and the postoperative course was complicated by a complete breakdown of the incision and evisceration, followed by secondary closure eleven days after the gastrostomy. The determination of the plasma ascorbic acid

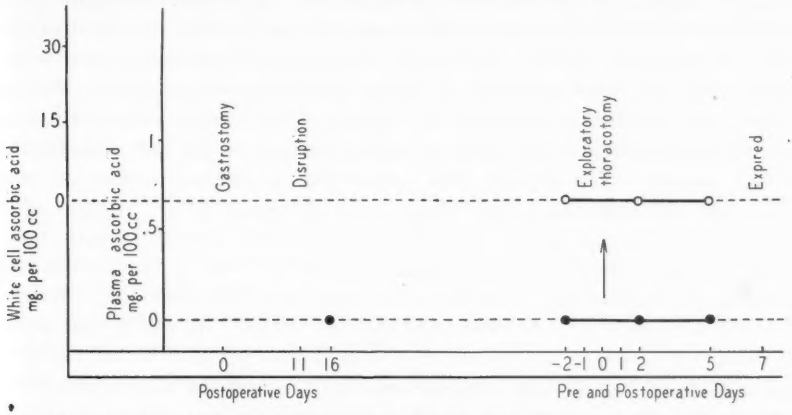

Fig. 6 (Case 5).—Complete absence of ascorbic acid in both plasma and white cells; wound disruption and death.

two days after the suture of the evisceration was zero. In the postoperative period the patient developed a bronchopneumonia and convalescence was slow but he was temporarily discharged sixty days after the first operation. He was readmitted Jan. 2, 1945, and during this time was given Blair's feeding and gained three pounds. An esophagectomy was planned and two days before the operation the plasma ascorbic acid level was still zero. An exploratory thoracotomy was performed Jan. 9, 1945, but the attempt to remove the esophagus was unsuccessful due to the fact that the tumor had extended to involve the mediastinal structure. Determinations of the blood ascorbic acid two and five days after the exploratory thoracotomy showed zero findings in both the plasma and white cell and platelets (Fig. 6). The patient died on the seventh postoperative day.

Comment.—This is a case in which a positive ascorbic acid deficiency should be considered an important factor in the wound disruption; this is the only patient found with zero ascorbic acid in the plasma and in the white cells and platelets, which signifies a state close to scurvy. Crandon, Lund, and Dill demonstrate that there is practically no scar formation in such a deficiency of ascorbic acid. It is thought that all patients with stenosis of the esophagus should be carefully studied with determinations of the plasma and white cell ascorbic levels. The amount of vitamin C they receive in their diet over a long period of time is not sufficient and the level in the blood and tissues is very low or may even be zero. If they are operated upon in such a prescorbutic state there is the possibility of absence of scar formation in all the operative field but especially at the level of the gastroesophageal anastomosis resulting in an esophago-

pleurocutaneous fistula or mediastinitis, two very common complications after esophageal resections.

The determination of the ascorbic acid content of the tissues appears to be the most adequate test to determine the saturation level of the patient. Bartlett, Jones, and Ryan[6] showed wide variations in the ascorbic acid content of guinea pig tissues according to a high or low intake of ascorbic acid. On a high ascorbic acid diet, the vitamin C content of healing wounds is considerably greater and their tensile strength is greater than the scars of scorbutic animals. The abdominal wall adjacent to the scar also shows a considerable rise, and a slight increase is found even at a distance from the wound. If the animal is maintained on a scorbutic diet during two weeks, no essential increase in ascorbic acid in the healing area is found, and a slightly lowered value in the remainder of the abdominal wall is observed, compared with the level in control biopsies, obtained at the time of the operation. The tensile strength of the wounds showing a high ascorbic acid content is much greater than that of those with low vitamin C values. The same authors studied also[7] the ascorbic acid content and the tensile strength of healing wounds in human beings, and concluded that "a sufficient depletion of vitamin C produces a decreased ascorbic acid content and tensile strength in healing wounds in the skin and fascia of human beings." The authors used patients with inguinal hernias on whom fascia lata was employed in the repair of the abdominal wall. "A strip of skin and a small extra amount of fascia lata were excised during the operation as control biopsy. An extra longitudinal incision of 2 cm. in length was made in the fascia lata parallel to its fibers and this was closed with silk. After ten days, the skin and fascia scar were removed and studied. In one of the patients, who had 0.08 and 0.09 mg. per cent of plasma ascorbic acid before the operation, a bilateral hernioplasty was performed. The first leg wound was allowed to heal without vitamin C therapy, other than the 100 mg. daily dose provided in the regular diet. During the ten-day healing period of the second leg wound, this dietary intake was supplemented by 100 mg. of ascorbic acid daily given by mouth. The tissue ascorbic acid level of the control biopsy of fascia taken at the time of the first operation was zero. During the ten-day healing period of this wound, the low plasma ascorbic acid level remained unchanged, and at the end of this time the excised fascia scar still showed an ascorbic acid value of zero and a tensile strength of only 300 Gm. or about one-fifth of normal (1,600 Gm.). The control biopsy of fascia from the second leg wound also showed a zero value for ascorbic acid. This wound was allowed to heal for ten days, 1,000 mg. of ascorbic acid being given orally each day in addition to the regular diet. The plasma ascorbic acid promptly rose to over 1.0 mg. per 100 c.c. At the end of ten days, the healing fascia scar was excised. Its ascorbic acid content was 5.73 mg. per 100 Gm., which is slightly lower than the average of 6.01 mg. per 100 Gm. noted in the other cases. The tensile strength of this fascia scar was 1,800 Gm., a figure slightly higher than the average of 1,600 Gm. for the other cases, and six times as high as that (300 Gm.) for the scar in the wound in the other leg, which healed without benefit of vitamin C therapy."

The ascorbic acid of the lung and muscles of some of the patients was tested. About 4.0 Gm. of these tissues were removed during the operation and the ascorbic acid was tested almost immediately. The muscle tissue is one of the poorest in the body. Bessey and King[9] and Giroud[13] evaluated the normal

amount of ascorbic acid in the muscle at about 4.0 mg. per 100 Gm. The determinations described in this paper were made in the muscle of seven patients, all of whom had lobectomies or pneumonectomies and the sections of tissue were removed during the operation. The following results were found: 0.25 mg. per cent in four patients, 0.30 mg. per cent in one patient, 0.45 mg. per cent in one patient, and 1.44 mg. per cent in one patient. There was, therefore, an average of only 0.31 mg. per cent.

In lung tissue, the normal amount was estimated by Yavorsky, Almaden, and King[52] as about 4.5 mg. per cent in patients between 46 to 77 years of age and 6.5 mg. per cent in those between 11 and 45 years of age. In the cases reported in this communication 3.41 mg. per cent (68 years old), 5.94 mg. per cent (14 years old), and 4.5 mg. per cent (64 years old) were found. This amount of ascorbic acid should be considered low because the tissues with scars and inflammation usually should have a higher amount than the normal ones.

One of the patients received 1 Gm. of ascorbic acid during four days before a left total pneumonectomy, and 6.0 mg. per cent in the muscle (latissimus dorsi) and 30.0 mg. per cent in the lung tissue were found; as only one patient was tested in this way, no general conclusion could be drawn. The day before the operation this patient had 0.80 mg. per cent in the plasma and 40.0 mg. per cent in the white cell platelets.

CONCLUSION

1. The closure of the bronchi after partial or total resection of the lung, and the gastroesophageal anastomosis still constitute two important problems in thoracic surgery; defective cicatrization frequently occurs in both cases, resulting in a bronchial or esophageal fistula.

2. The surgical technique employed in the procedure is very important in the prophylaxis of these complications and in obtaining a good scar, but the technique constitutes only one of the factors influencing scar formation. Arey,[2] in 1936, enumerated twelve different important factors in scar formation and many of these have been underestimated in the prophylaxis of bronchial or esophageal fistula. In many cases it is impossible to obtain a good suturing because of local conditions, but even with the best technique the disruption of the sutures due to lack of scar formation may occur.

3. The amount of ascorbic acid in the blood and in the tissues has been considered one of the most important factors in the formation of the intercellular collagenous tissue, and in the strength of the scar, both in animals and in human beings. The amount of ascorbic acid in some patients was studied before and after lobectomy, pneumonectomy, and esophageal resection. The blood proteins of these patients were tested continuously because hypoproteinemia is another important factor in scar formation and should always be corrected.

4. The chest condition which brings the patient to the hospital may be responsible for a low plasma ascorbic acid level before the operation. In twenty-two patients examined, the average obtained was 0.15 mg. per cent (normal 0.8 to 1.2). Only one patient had a normal level before the operation and nine patients showed complete absence of ascorbic acid in the plasma.

5. The operation by itself reduces considerably the plasma ascorbic acid, according to the severity of the surgical procedure. This level remains low during a long or short interval according to the postoperative complications and treatment.

6. It is possible to maintain an almost normal plasma ascorbic acid level before and after the operation with the administration of 1,000 mg. of ascorbic acid every twenty-four hours.

7. The determination of the white cell platelets ascorbic acid gave different results in different patients. When the general condition was good and the patient was a good risk the white cell platelet level did not change with the operation, even when the plasma level was zero. In one patient with esophageal cancer and artificial alimentation through a gastrostomy the plasma and white cell platelets were both found deprived of ascorbic acid, a condition which represents a prescorbutic state without clinical evidence.

8. The amount of ascorbic acid in muscle and lung tissue removed during the operation seems to be below the values considered as normal by different authors.

9. Every patient with chronic surgical chest conditions should be given high doses of ascorbic acid before and especially after important surgical procedures.

I wish to express my gratitude to Dr. Evarts A. Graham who suggested to me the idea and the general plan of this work and to Dr. Ethel Ronzoni of the Department of Biochemistry who taught me the method of Mindlin and Butler for the quantitative determination of ascorbic acid and assisted me greatly in the chemical studies.

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TUMOR OF THE LUNG DUE TO CRYPTOCOCCUS HISTOLYTICUS (BLASTOMYCOSIS)

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INFECTION with certain yeastlike fungi, the blastomyces, may produce local lesions, involving the skin and bones, or becoming generalized, produce lesions in the internal organs, of which the lungs are involved most frequently. The lungs have been considered as the common portal of entry in systemic disease. Until recently most of the pulmonary cases have been reported from Chicago or its vicinity, but it undoubtedly occurs in other parts of the world. The pulmonary lesions consist of broncho-pneumonia, miliary nodules, abscesses, areas of consolidation and fibrosis. The pleura and pericardium may also be involved in the pathologic processes. . . . Pulmonary involvement alone during the whole course of the disease must be exceedingly rare, if it has ever been observed at all. . . .''[1] From the literature available to us, we have been unable to find any reference to tumor formation in the lung being caused by the blastomyces.

''At present, blastomycosis may be caused by (1) Saccharomycetaceae, and (2) two genera of the blastosporineae, which are hyphomycetes, the so-called cryptococcus. The outstanding species in this group pathogenic to man are the *Cryptococcus capsulatus* (Darling, 1906), the cause of the very fatal 'histoplasmosis,' *Cryptococcus hominis* (Vuillemin, 1901), causing the type of blastomycosis described by Busse-Buschke, the Old World form of the disease, and *Cryptococcus histolyticus* (Stoddard and Cutler, 1916), the cause of a not uncommon cerebro-spinal meningitis.''[2]

The patient reported here presented a large solitary lung tumor due to the *Cryptococcus histolyticus.*

CASE REPORT

The patient, S. M., a native male child of 12 years, employed as a laundry boy, was admitted to King George V Hospital for Tuberculosis complaining of cough and sputum of about four months' duration. His illness began with headache and generalized pains, followed soon after with cough and mucoid sputum. At the time of admission the cough had become much less and there was hardly any sputum. There was no hemoptysis, no chest pain, and no dyspnea on exertion. He complained of night sweats, and loss of appetite, energy, and weight. There was no history of any contact with sheep or dogs at home. The previous history was irrelevant. There was no family history of chest trouble.

Examination.—General condition was good. Weight was 86 pounds, temperature, 99 to 100° F.; pulse, 80 to 110; respiration, 20. Visible mucous membranes were pale and the tongue was furred. There was slight clubbing of the fingers, but no adenopathy nor evidence of any past or present skin lesion.

Respiratory System.—There was diminished movement of the chest on the right side and dullness of the right upper chest anteriorly and in the right axilla. Breath sounds were absent in the area of dullness. There were distant breath sounds posteriorly.

Cardiovascular System.—Nothing abnormal was found. The heart was not displaced. Blood pressure was 118/70.

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Alimentary, Genitourinary, and Central Nervous Systems.—Nothing abnormal found.

Investigations.—Blood examination: Hemoglobin, 70 per cent; total white blood cells, 18,200 per c.mm.; differential: polymorphonuclears, 60 per cent; eosinophiles, 12 per cent; lymphocytes, 23 per cent; monocytes, 5 per cent; and red blood cells, 4,370,000 per c.mm. Blood Wassermann was negative, tuberculin patch test, positive (after 96 hours); Casoni skin test, negative; urine, clear; and sputum, mucoid, negative for tubercle bacilli or other pathogens.

X-ray of Chest.—A large rounded tumor showed in the right lung (Figs. 1 and 2). On bronchography no lipiodol entered the area of the tumor.

A diagnostic right artificial pneumothorax was done and a good collapse was obtained showing the tumor to be intrapulmonary (Figs. 3 and 4). An exploratory thoracotomy was advised, but the parents refused. The patient left the hospital against medical advice and was readmitted about three weeks later. On readmission, his general condition had deteriorated. Temperature was 98 to 102.4° F., pulse, 90 to 100; respiration, 20 to 24. He looked drawn and appeared to have lost some weight.

Fig. 1. Fig. 2.

Fig. 1.—On admission, Dec. 30, 1943, showing circumscribed tumor in the right lung.
Fig. 2.—Lateral radiograph of tumor shown in Fig. 1.

A radiograph of the chest at this time showed an increase in the size of the tumor, and obliteration of the right artificial pneumothorax (Fig. 5). An exploring needle was inserted into the tumor, but nothing was withdrawn. The tumor on exploration felt rubbery hard. An attempt was made to reinduce the right artificial pneumothorax, but without much success, the pleura feeling thickened and adherent. A later radiograph showed an increase in the size of the tumor with displacement of the heart to the left (Fig. 6).

The parents eventually consented to an operation, and he was prepared for a pneumonectomy. His blood count was: Hemoglobin, 55 per cent; total white blood cells, 12,200 per c.mm.; differential: polymorphonuclears, 67 per cent; eosinophiles, 10 per cent; lymphocytes, 15 per cent; monocytes, 8 per cent, and red blood cells, 4,140,000 per c.mm. He was given a preoperative blood transfusion.

Operation (Dr. A. Radford and Dr. W. Phillips).—The operation lasted two and one-half hours. Under intratracheal cyclopropane anesthesia (Dr. H. Grant-Whyte), an incision was made along the seventh rib on the right side. The rib was removed and the

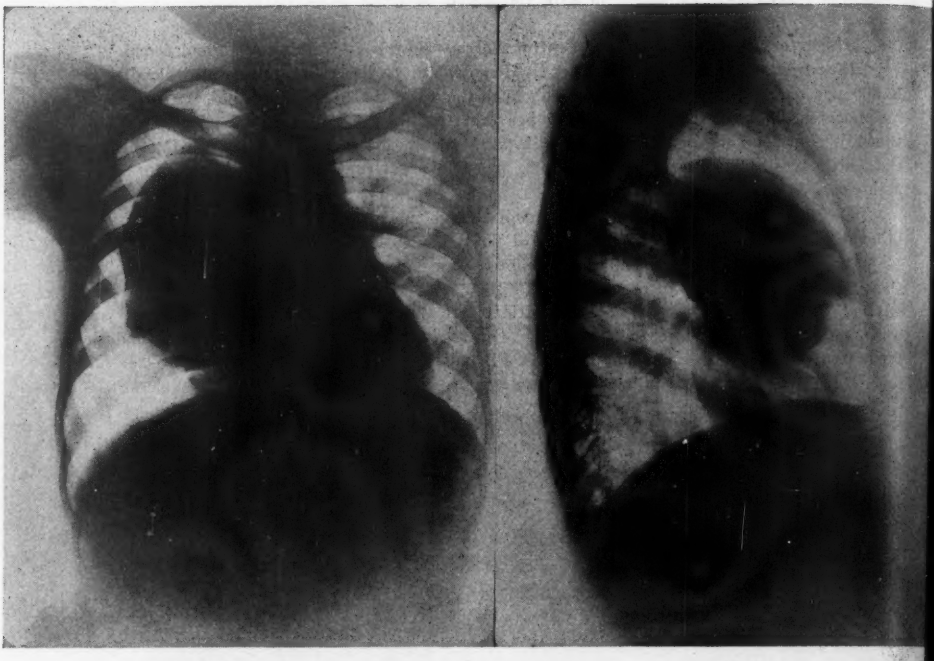

Fig. 3. Fig. 4.

Fig. 3.—Jan. 19, 1944, after diagnostic pneumothorax, showing the intrapulmonary nature of the tumor.

Fig. 4.—Lateral radiograph of tumor shown in Fig. 3.

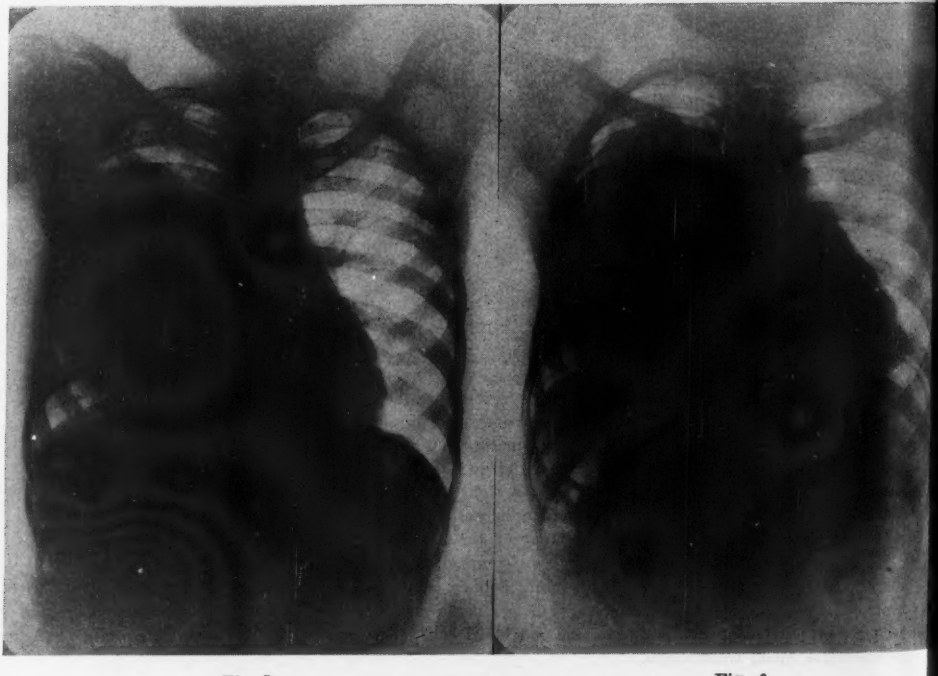

Fig. 5. Fig. 6.

Fig. 5.—Feb. 14, 1944, after readmission, showing increase in size of tumor. Compare with Fig. 1.

Fig. 6.—March 30, 1944, preoperative radiograph, showing some displacement of the heart to the left.

pleura incised. The pleural cavity was almost entirely occupied by a large hard rounded mass, adherent to the chest wall on its posterolateral surface. Several thick band adhesions were divided with difficulty and it was possible to insert a hand round the tumor. Several troublesome bleeding points were controlled and ligatured. On account of the size and immobility of the tumor it was impossible to visualize the root area and dissection pneumonectomy was, therefore, impossible. Lung tourniquets were placed around the lung root by touch and the root divided between the two tourniquet cords. On removal of the mass, it was found that only an upper and middle lobectomy had been done, the lower lobe lying compressed inferiorly, but containing no evidence of infiltration. It was, therefore, left in situ. There was no evidence of involvement of the mediastinal glands. The individual constituents of the ligatured hilum were sutured separately with silk. The lower lobe was then slowly inflated; the ribs were approximated and the wound closed.

Fig. 7.—Operation specimen. The tumor (on the left) after enucleation from the upper and middle lobes shown alongside. Some shrinkage has occurred following fixation in formol-saline.

A large intercostal drainage tube was inserted posteriorly for underwater drainage. During the operation the patient had to be given two pints of blood and two pints of intravenous saline. His general condition on leaving the operating room was poor.

On examination of the operation specimen, the tumor mass was found to be hard, fibrous, and slightly lobulated in contour and was easily enucleated from the lung lobes to which it was attached. It weighed one and one-half pounds (Figs. 7 and 8).

Histology of Tumor of Human Lung.—The specimen showed the structure of a granuloma. It was composed of irregular spaces separated from one another by thin, delicate walls.

The walls were formed of fibroblasts and histiocytes. The histiocytes contained lipoid material but after passing through fat solvents they presented a "foamy" appearance (see Fig. 9).

There was also patchy infiltration of the walls by eosinophile and neutrophile polymorphonuclear leucocytes.

The irregular spaces contained one or more yeastlike bodies, some of which showed evidence of budding. These yeast bodies (cryptococci) were round in shape and consisted of a highly refractile limiting membrane which was surrounded in turn by a broad capsule of hyaline mucoid material (see Fig. 10).

The cryptococci proper without the mucoid capsule measured from 3 to 4 mμ in diameter.

This organism was morphologically indistinguishable from the *Cryptococcus histolyticus* (*Torula histolytica*).

The neutrophile polymorphonuclear reaction being in lung tissue was probably due to secondary infection.

Progress.—There was a fair amount of bloodstained discharge from the intercostal drainage tube in the first twenty-four hours, after which it was removed. The patient had a temperature of 98 to 102.4° F. His general condition improved, but the temperature persisted. The wound healed by first intention; breath sounds became audible on the right side of the chest, and portable x-rays of the chest showed the expanded lower lobe occupying

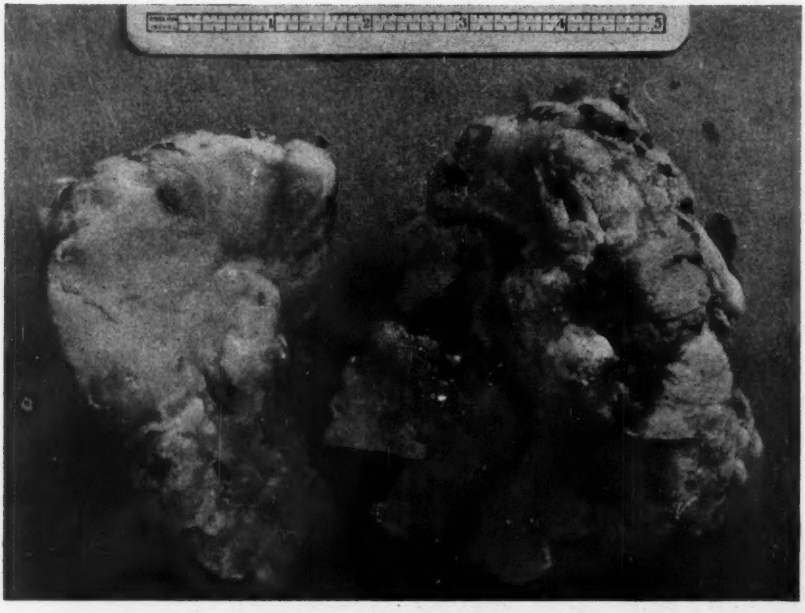

Fig. 8.—The tumor on section showing its lobulated contour and the homogeneity of its cut surface.

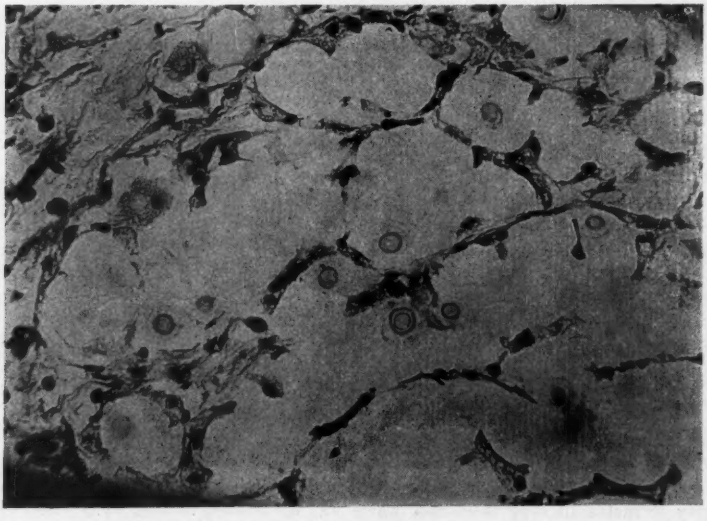

Fig. 9.—Photomicrograph of human lung lesion. It shows irregular spaces and thin limiting walls which constitute the granuloma. The cryptococci are seen lying free in the spaces. (Magnification ×480.)

the right hemithorax. He had no cough nor sputum. He was given a course of sulfadiazine with no effect on the temperature. On the twenty-third postoperative day he complained of severe frontal headaches and photophobia. Examination showed signs of meningitis. A lumbar puncture was made and the cerebrospinal fluid was slightly hazy and under distinct pressure. On microscopic examination, the fluid showed a marked polymorphonuclear exudate, but no organisms were seen. A full course of sulfadiazine had no effect on the temperature

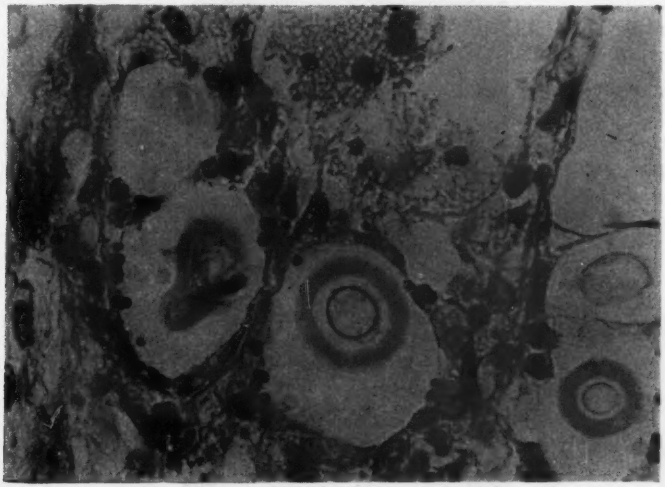

Fig. 10.—Photomicrograph of human lung lesion. The cryptococci are seen lying free in the spaces formed in the granuloma. They consist of a highly refractile limiting membrane surrounded by a zone of hyaline mucoid material. (Magnification ×1000.)

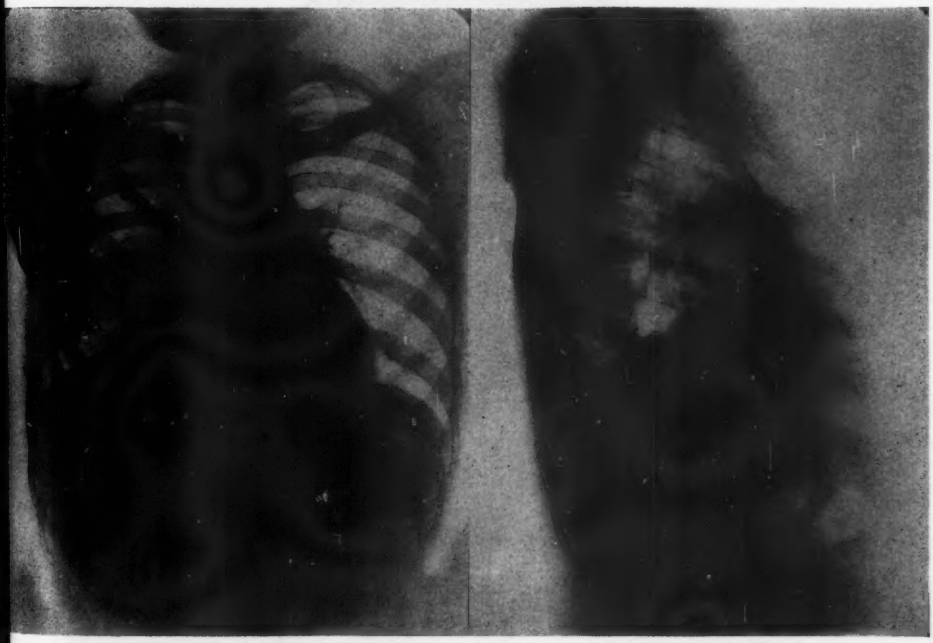

Fig. 11. Fig. 12.

Fig. 11.—July 5, 1944, postoperative radiograph, taken one and one-half months after discharge, showing expanded lower lobe completely occupying the right hemithorax.

Fig. 12.—Lateral radiograph of chest shown in Fig. 11.

nor the meningitis. Because of the possibility of the meningitis being related to the original etiologic agent giving rise to the tumor (*Cryptococcus histolyticus*), he was given large doses of potassium iodide (90 gr. a day), and four days later the temperature returned to normal for the first time since admission to the hospital four and one-half months previously. He lost all signs and symptoms of meningitis and was discharged fit two weeks later. Figs. 11 and 12 are radiographs of the chest taken after discharge from hospital.

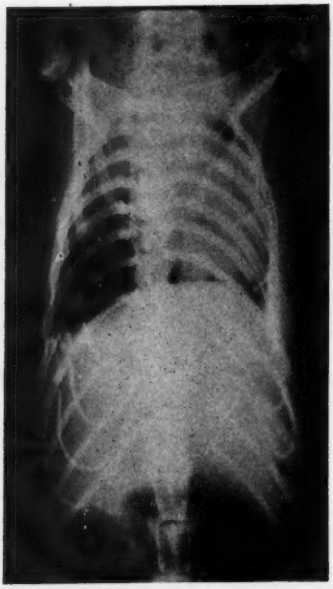

Fig. 13.—Postero-anterior radiograph of guinea pig showing haziness of right lung.

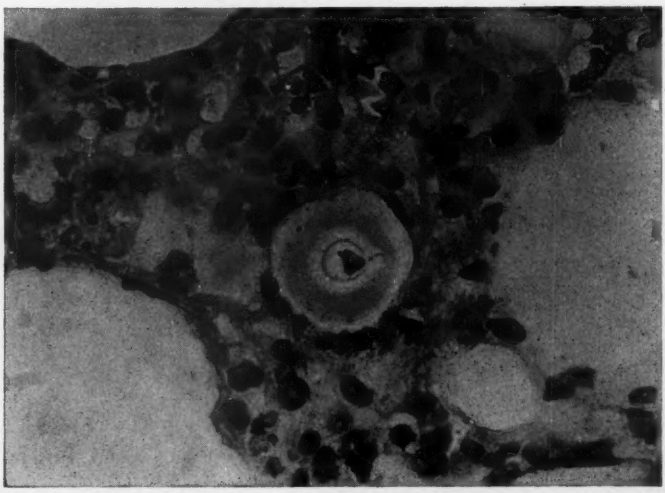

Fig. 14.—Photomicrograph of guinea pig lung lesion. A single cryptococcus is shown embedded in the interstitial inflammatory tissue. The organism is in the process of budding and is similar in other respects to the organism shown in the human lung lesion. (Magnification ×1000.)

One cubic centimeter of centrifuged cerebrospinal fluid, which had been withdrawn by lumbar puncture, was injected into the right lung of a guinea pig under strict aseptic precautions. The guinea pig died fifty-two days later.

X-ray showed a generalized haziness of the right lung (Fig. 13), and at autopsy the right lung felt consolidated. The organs were removed and sent in toto for pathologic examination.

Guinea Pig Tissue (Lung).—Sections of the lung of this guinea pig showed the presence of small but widespread areas of interstitial chronic inflammation in which yeastlike bodies were embedded. These yeast bodies were also widely distributed throughout the animal lung tissue and occurred in the inflammatory tissue either singly or in groups up to about six in number. Many of them showed evidence of budding and were surrounded by a broad zone of hyaline mucoid material (see Fig. 14).

These organisms presented the morphologic characters of the *Cryptococcus histolyticus* and were identical with the organisms found in the human lung lesion.

No cryptococci were found in any of the other animal tissues examined.

SUMMARY

A case is presented of a tumor of the lung due to blastomycosis (*Cryptococcus histolyticus*) successfully removed at operation.

This case shows many interesting features not the least of which is the reproduction of the disease in the guinea pig. It is clear from the experiment that the meninges of the patient was also the site of the cryptococcus infection. The response of this secondary meningitis to large doses of potassium iodide is striking. It is interesting to speculate on the effect on the tumor had large doses of potassium iodide been given before the operation.

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OCCLUSION OF THE SUPERIOR VENA CAVA DUE TO SYPHILITIC MEDIASTINITIS

Collateral Circulation After Nineteen Years

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INTRODUCTION

THE remarkable capacity of the venous system to adapt itself to changing pressures, resulting from either partial or complete obstruction, has been studied in the past from clinical, pathologic, and experimental viewpoints. That occlusion of the great veins of the thorax is compatible with life, if time is afforded for the development of a collateral circulation, has been well known for many years.[1] The case reported here, while exhibiting a remarkable picture and raising interesting questions relating to pathogenesis, is chiefly worthy of record because it illustrates so well the value of the newer methods of studying cardiovascular dynamics in elucidating problems arising from mediastinal obstruction of the venous system.

CASE REPORT

Dec. 17, 1925, W. C. H. (Mt. S. M. No. 262198), a man aged 49 years, was admitted to the Mount Sinai Hospital and placed on the medical service of Dr. B. S. Oppenheimer. During his hospital stay he was under my observation and I later presented the case at the monthly clinical conference of the hospital in February, 1926.

For six months prior to his seeking admission, the patient had become aware of increasing swelling of the head and neck, extending down to the shoulders. He had noted that the edema was most noticeable on arising in the morning and seemed to diminish during the course of the day. No cough, dyspnea, or dysphonia had been noted. In the past he had had pleurisy with effusion at the age of 22 years. Gonorrhea and syphilis were contracted when he was 24 years old. "Mixed" treatment had been administered for only a few months. As recently as two years before admission, his complement fixation reaction (Wassermann) was positive (2 plus).

On physical examination the patient was found to be a well-developed and well-nourished white man, lying propped up in bed, with cyanosis and edema of the face and neck, but breathing easily. Numerous dilated veins were noted over both lateral chest walls and the anterior aspect of the chest and abdomen. The heart and lung examinations disclosed no abnormalities. A scar, such as results from the healing of a chancre, was found on the glans penis. The blood count was as follows: hemoglobin 102 per cent, white blood cells 6,500, of which the polymorphonuclear leucocytes numbered 65 per cent, and the lymphocytes 35 per cent. The blood pressure was identical in both arms, 118 mm. systolic, 78 mm. diastolic. The blood complement fixation test (Wassermann) was strongly positive (4 plus).

Under observation the edema of the face and neck increased, and both upper extremities became swollen. The cyanotic edematous appearance of the upper part of the body contrasted sharply with the normal appearance of the abdomen and legs. Dysphonia was noted on the fourth day of his stay in the hospital but no paralysis of the vocal cords was found. Roentgen examination of the chest disclosed marked thickening of the pleura at the right apex. Extending down along the mesial portion of the right upper lobe was an area of fibrosis, interpreted as being due to an old tuberculous process with displacement of the mediastinum to the right side. A second examination, twelve days later, showed no changes. In neither plate was there evidence of mediastinal neoplasm or aortic aneurysm. For this reason, clinical opinion leaned strongly to a diagnosis of syphilitic mediastinitis and obstruction of the superior cava in spite of the rarity of this conditon. A diffusely infiltrating

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neoplastic process causing pressure on the great veins of the superior mediastinum was also considered as a diagnostic possibility.

With the discovery of the positive Wassermann reaction, treatment was initiated with the administration of mercury salicylate by intramuscular injection and potassium iodide by mouth. Later bismuth salts were substituted for the mercury salicylate. The patient's condition, however, continued to grow worse and, in the belief that the mediastinum might be the site of a roentgen-sensitive infiltrating process, one treatment with high voltage roentgen rays was directed toward the retromanubrial space.

Twenty-four hours later the patient's temperature began to rise, and the second day following the treatment, a large area of redness appeared in the skin of the anterior chest wall as well as of the right shoulder and right arm. This skin lesion was diagnosed at that time as erysipelas, unrelated to the roentgen-ray treatment. In retrospect it seems possible that this skin lesion should be grouped with those rapidly appearing roentgen-ray reactions in the skin which are believed to be in part allergic in nature.[2] For several days the patient was critically ill, the temperature being maintained at 103°F. As the "erysipelas" diminished in intensity, the edema of the patient's face and neck subsided partially, his general condition improved, and Jan. 21, 1926, he was discharged to the care of his own physician.

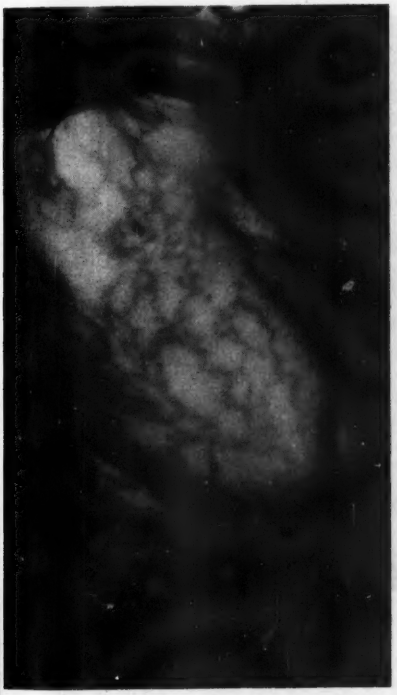

Fig. 1.

Fig. 2.

Fig. 1.—Infrared photograph of right side of torso.
Fig. 2.—Infrared photograph of left side of torso.

Active antisyphilitic therapy was continued regularly for several years, even after the Wassermann reaction became negative. The patient resumed his occupation as night clerk in a hotel, and had observed no change in his functional capacity until a short time before he again came under my observation (November, 1943). Large varices appeared on the lateral aspects of his body following his discharge from the hospital but have not increased in size appreciably in recent years. His only complaint referable to the venous obstruction was a feeling of fullness and throbbing in the head when bending over. He slept on three pillows of ordinary size. Of late he had been annoyed by precordial pain and dyspnea on exertion. It was for relief of these symptoms that he again sought me out; my surprise, at seeing him alive after eighteen years, can easily be understood.

On re-examination after this long interval, the patient was found to be a ruddy-faced elderly man, with pendulous abdomen, mentally alert, quick and accurate in responding to questions. The enlargement and the multiplicity of the superficial veins at the base of the neck, and on both sides of the chest and abdomen, were amazing (Figs. 1 and 2); tortuosity was marked, and anastomoses frequent. That the blood flow was from above downward could be easily demonstrated. Inspiratory filling of the veins of the neck was readily made out. None of the venous channels showed evidence of either inflammation or thrombosis. The heart was enlarged to the left; the sounds were of good quality, but distant; a soft systolic murmur was heard at the apex, but was not transmitted. The lungs were clear. The abdomen, although pendulous, disclosed no visceral enlargement or palpable masses. Pupillary reactions were normal and the knee jerks active. The blood pressure was 200 mm. systolic, 108 mm. diastolic.

Roentgenogram examination of the chest was reported as follows: There was slight increase in the width of the superior mediastinum, and the apical pleura on both sides showed moderate thickening. In addition there was thickening of the interlobar fissure on the right side where a few pleural calcifications were also noted. The pleura over the entire right lung seemed somewhat thickened. Fibrosis in the right lower lobe was observed. The heart showed left ventricular enlargement (Fig. 3).

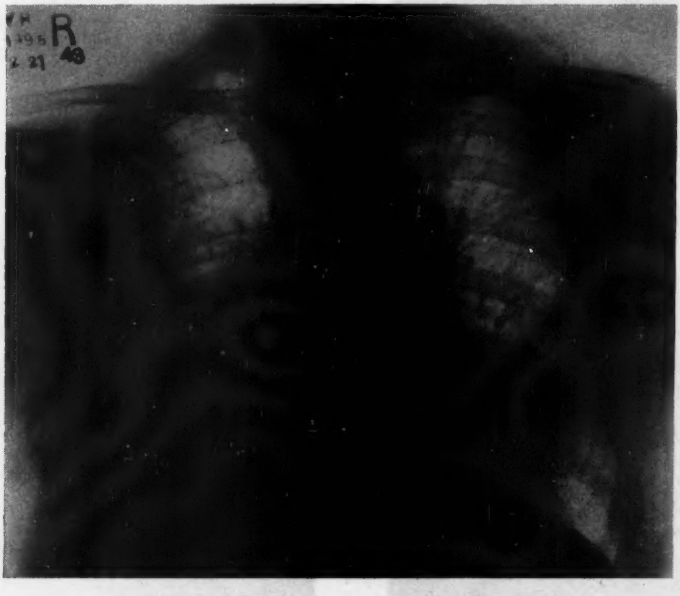

Fig. 3.—Roentgen-ray photograph of chest.

Routine examination of the urine was negative. The blood count was normal. The blood Wassermann reaction was negative. The electrocardiogram showed normal rhythm, left ventricular preponderance, normal QRS complexes, and a diphasic T_1.

Compared with his status when seen eighteen years before, he presented the picture of a superior vena cava obstruction well compensated by an extensive collateral circulation. The roentgen-ray picture of the upper mediastinum had not changed. The blood complement fixation reaction had become negative. The recent development of essential hypertension and arteriosclerotic heart disease with symptoms of coronary insufficiency seemed to be unrelated either to the syphilis or to the mediastinitis, since hypertensive cardiovascular disease is common in individuals in the seventh decade of life.

SPECIAL STUDIES

Lian and Abasa,[3] Carlson,[4] and Hitzig[5] have emphasized the changes in the venous pressure of the upper extremities in cases of superior vena caval obstruction. In this patient the venous pressure was 22 cm. of blood in the left

antecubital vein, and only 9.5 cm. in the femoral vein. The circulation time (arm to tongue) from the right arm was 46 seconds, with a weak end point, and 19 seconds from the right femoral vein, with a strong end point. In addition it should be noted that application of a tourniquet to the thorax to occlude the lateral thoracic veins caused a sharp rise in the venous pressure in the arm.

Hitzig has emphasized that inspiratory filling of the neck veins may occur in congestive heart failure, constrictive pericarditis, and superior vena cava obstruction. The rise in venous pressure in the arms on application of a thoracic tourniquet occus only in superior caval obstruction, because of the interference with the superficial venous blood flow downward to the inferior vena cava (Fig. 4). It indicates also that the vena caval obstruction is located close to the heart, either below or including the orifice of the vena azygos major.

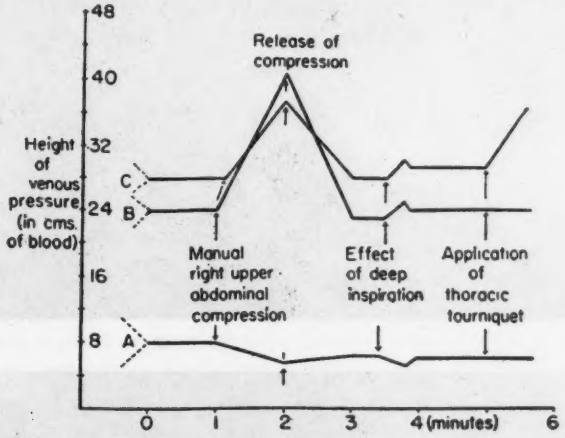

Fig. 4.—Cervical venous pressure curves in (*A*) normal individuals, (*B*) right heart failure (combined) of marked degree, and (*C*) superior vena cava obstructions (below azygos vein). In superior vena caval obstruction (below azygos vein), manual compression of right upper abdomen, application of thoracic tourniquet, and deep inspiration will cause rise of the cervical venous pressure due to interference with the collateral pathway through the inferior vena cava. (From Hitzig, W.: J. Mt. Sinai Hosp. 8: 625, 1942.)

Further information of value was obtained by taking roentgenograms of the chest after the injection of 70 per cent diodrast solution into the antecubital veins according to the method of Sussman, Steinberg, and Grishman.[6] The results are well shown in Figs. 5 and 6. On the right side we see the contrast medium sharply visualizing the brachial and axillary veins, the greatly enlarged lateral thoracic venous plexus, the subclavian and right innominate veins, and a portion of the left innominate vein. Entering the right innominate, the vena azygos major can be traced downward close to the right border of the heart where it divides into two trunks. The diodrast column abruptly terminates in the superior vena cava below the origins of the azygos major and the left innominate veins. Whether the area of lessened density noted in the right innominate vein is due to technical factors or to a relative stenosis cannot be determined. A similar area of diminished density is to be noted in the first portion of the azygos major. Numerous small venous channels in the chest wall are readily seen against the background of the lower part of the right lung field.

On the left side, diodrast injection reveals again the origin of markedly enlarged lateral thoracic plexuses from the axillary vein, with abrupt termination of the vascular visualization in the subclavian vein. We are forced,

Fig. 6.

Fig. 5.

Fig. 5.—Roentgen-ray photograph of chest after injection of diodrast solution into right antecubital vein.
Fig. 6.—Roentgen-ray photograph of chest after injection of diodrast solution into left antecubital vein.

therefore, in reconstructing the total picture from the results of right-and left-sided venography, to postulate an area of complete or partial stenosis of the distal portion of the left innominate vein and of part of the subclavian vein. Such separated areas of obstruction in the great mediastinal veins are to be explained either on the basis of focal areas of maximum pressure resulting from external disease, or as due to recanalization of once thrombosed portions of the veins.

These studies indicate the completeness of the caval occlusion, but are surprising in showing, in addition, the partial narrowing of some of its branches. It is clear from both the clinical observation and the special studies that the blood flow from the head, neck, upper extremities, and upper portion of the chest is chiefly by way of the extensive superficial collateral circulation and the vena azygos major, in which the direction of the flow is reversed, into the inferior vena cava and thence into the right auricle. The patency of the azygos major, while insufficient to carry the entire venous return from the upper part of the body, relieves the superficial venous collaterals of part of their burden, and accounts in part for the benign outcome of the disease in this individual. For an excellent diagrammatic study of the collateral circulation in obstruction of the superior cava, the reader is referred to Blasingame's[7] paper.

PATHOGENESIS

Obstruction of the superior vena cava is not a common occurrence, and thrombosis of this vessel is an actual rarity, both clinically and pathologically. Because of the interest aroused by these unusual cases there is a rich literature on the subject, comprising many case reports, several dating back almost two centuries, and two recent analytical reviews of great value. In 1934, Ehrlich, Ballon, and Graham[8] collected and analyzed 309 cases of superior caval obstruction, emphasizing the benefit in certain instances of mediastinal decompression for the relief of symptoms. Ochsner and Dixon[9] in 1935, reviewed and discussed the literature of superior caval thrombosis only, studying 120 cases from other authors together with two of their own.

In this series thrombosis was found to be due to phlebitis in 44 cases (36.6 per cent), to external compression in 35 cases (29.1 per cent), to mediastinitis in 28 cases (23.3 per cent), and to unknown causes in 13 (10.8 per cent). "Syphilis was responsible either directly or indirectly in 40 (33.3 per cent) of the 120 cases; 12 had luetic phlebitis, 11 luetic mediastinitis, and 17 aneurysm. Tuberculosis caused the thrombosis in 14 (11.6 per cent) with tuberculous mediastinitis in 10 and phlebitis in 4. There was an associated heart disease in 10 (8.3 per cent). Pyogenic infections were responsible in 8 (6.6 per cent), 7 having phlebitis and 1 mediastinitis. Trauma was an etiologic factor in only 2 cases (1.6 per cent), 1 with mediastinitis and the other with phlebitis."[9]

It is evident from the foregoing that, leaving out aneurysms, syphilis is an important causative factor in mediastinitis and also in phlebitis of the superior vena cava leading to thrombosis of that vessel. In the cases reported by Faure,[10] by Comby, Vigoroux, and Collet,[10] by Beevor,[10] and by Gossage,[10] the diagnosis of syphilis seems to have been well founded. Martland[11] and Keefer[12] have also emphasized the importance of syphilis. Erganian and Wade,[13] in a report of three cases of chronic fibrous mediastinitis, have seriously questioned the validity of the evidence for both tuberculosis and syphilis in previously reported cases, alleging that the diagnosis of tuberculosis has depended on the

demonstration of calcified nodules in tracheal nodes, a common post-mortem finding. They continue: "The support for the concept of syphilitic mediastinitis rests on even more insecure grounds. There is usually nothing more than a positive Wassermann, and it is a well-established principle that not all the individual lesions in a patient with syphilis are of necessity caused by the spirochete." On the other hand, they do advise specific therapy in patients with syphilis. For their own cases they prefer the designation, "chronic fibrous mediastinitis," which they believe to result from a mild mediastinal inflammation in an individual with a tendency to excessive cicatrization which slowly progresses to form the typical dense mass of fibrous tissue. This mass is made up of dense collagenous tissue with foci of infiltration with lymphocytes and calcification.

Strict adherence to such rigid criteria of diagnosis would eliminate entirely the idea of a syphilitic mediastinitis since even a biopsy at the height of the disease might fail to show lesions of undoubted specificity.

While too facile association of unrelated findings may be evidence of wishful clinical reasoning, it is also possible to be too rigorous in establishing diagnostic criteria. Careful clinical and pathologic correlation is the ideal, but in the absence of post-morten findings one is forced to base the diagnosis on the available clinical data, carefully analyzed in the light of experience and considered according to the principles of the scientific method. In the case herewith reported, syphilis is considered to have been present because of the history, the penile scar, and repeatedly positive complement fixation reaction in the blood. In view of the long-standing reversal of the Wassermann reaction following specific therapy over a period of years, and associated with clinical improvement, there seems no valid reason to look for causes other than syphilis to explain the total clinical picture. The attack of high fever and the skin reaction suffered by the patient following high voltage roentgen-ray exposure probably affected the mediastinal process in a nonspecific manner, in much the same way as hyperpyrexial treatment benefits cases of syphilis of the central nervous system. The chain of clinical evidence for syphilis as the basic causative agent in this patient seems as complete as can be expected under the most favorable circumstances.

Actually even post-mortem examination of scar tissues resulting from a treated or a self-healed syphilitic process will give but little definite proof of syphilis. In the patient reported by Comby and his associates, where caval obstruction had been observed over a fifteen-year period, death was due to general paresis. At post-mortem a thick mass of fibro-adipose tissue was found behind the manubrium, intimately adherent to the pericardium and to the adventitia of the great vascular trunks, and firmly uniting all the organs of the anterior mediastinum, without altering their relations. Freed of the adhesions, the aorta and its branches, the pulmonary artery and its branches, the pulmonary veins, as well as the trachea and bronchi appeared healthy. On the contrary the vena cava superior, the subclavian and axillary veins were transformed into fibrous cords of reduced size, resembling tendons. Histologically the vena cava superior was seen to be obstructed by an organized and partially calcified thrombus. The retrosternal tissues were made up of dense fibrous bands containing isolated collections of round cells.

The resemblance of this histologic picture to that described by Erganian and Wade in their nonspecific cases makes it clear that one cannot rely upon pathologic findings to differentiate between the two types of mediastinitis.

That in certain cases one is forced to postulate an unknown or nonspecific cause is not disputed but, to me, it seems equally evident that in other cases, surely not numerous because of the rarity of the condition due to any cause, the implication of syphilis as the etiologic agent is thoroughly justified on clinical grounds.

The sequence of events in the case on which this report is based, is believed to be first, infection of the mediastinal tissues by *Treponema pallidum;* second, slow proliferation of these tissues (six months elapsed between onset of thoracic symptoms and the patient's admission to the hospital); third, gradual compression of the vena cava superior and its branches; fourth, secondary thrombosis of these venous trunks. This process, proceeding slowly over a period of more than six months, gave ample time for the development of an adequate collateral circulation. In Comby's case the thrombotic process extended so far into the axillary and jugular veins that the thrombosed veins became palpable, a clinical observation which led to the proper diagnosis.

Ochsner and Dixon have stressed the diagnostic importance in superior caval obstruction of edema of the head and face, occurring when the patient is in the recumbent position and slowly disappearing when the erect position is assumed. I was able in another patient, on the basis of this symptom alone, to make the correct diagnosis. To-day, the measurement of differential venous pressures and circulation times, together with diodrast studies of the venous trunks, makes possible an extremely accurate clinical diagnosis.

That the prognosis as to life in some of these cases is good may be concluded from the finding of the condition in persons advanced in years. The man reported upon here is now 68 years old. Gossage's patient was 74 years old, and Blasingame's was aged 93 years. In this last instance the condition was found in the dissecting room and no clinical history was available; Blasingame did not find any evidence of a superficial collateral circulation. This observation seems to indicate that the deep veins alone are at times capable of establishing an adequate collateral circulation to overcome the obstruction. Veal's[14] paper on the mode of development of collateral venous circulation in the extremities is of value in understanding the underlying factors involved in this process. Sampson and his collaborators[15] have warned against laying too much stress on prominent chest veins as a sign of collateral circulation, since this prominence is seen at all ages and is extremely common after the age of 50 years. They believe that compression and partial obstruction of the subclavian vein between the clavicle and the first rib anterior to the scalene tubercle are the commonest cause of such prominent venous distention.

SUMMARY

1. Occlusion of the superior vena cava in a man, now 68 years old, has been described in its onset and after a nineteen-year interval.

2. The cause of the obstructive symptoms and signs has been explained on the basis of syphilitic mediastinitis with secondary venous thrombosis.

3. The diagnostic value of the measurement of venous pressures in the upper and lower extremities, as well as of the determination of the circulation times, has been emphasized.

4. The vivid localization of the sites of obstruction in the great thoracic veins and the striking visualization of the collateral circulation by venography are evident from the accompanying illustrations. Particularly noteworthy is the delineation of the vena azygos major due to the reversal of the blood flow.

5. From a clinical viewpoint, the presence of transitory edema of the head and neck, observable on arising in the morning and disappearing slowly after assuming the upright position, must be kept in mind as a pathognomonic sign of venous obstruction in the upper mediastinum. Confirmatory signs are to be sought in disturbances of the venous pressure and circulation time in the upper extremities.

I am indebted to Dr. B. S. Oppenheimer for permission to publish this case, to Dr. William Hitzig for the determination of the venous pressures and the circulation times, and to Dr. Marcy Sussman and Dr. Arthur Grishman for the venographic studies.

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